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 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  SEP 09   CA/CAplus records now contain indexing from 1907 to the
                   present
 NEWS  4  AUG 05   New pricing for EUROPATFULL and PCTFULL effective
                   August 1, 2003
 NEWS  5  AUG 13   Field Availability (/FA) field enhanced in BEILSTEIN
 NEWS  6  AUG 18   Data available for download as a PDF in RDISCLOSURE
 NEWS  7  AUG 18   Simultaneous left and right truncation added to PASCAL
 NEWS  8  AUG 18   FROSTI and KOSMET enhanced with Simultaneous Left and Righ
                   Truncation
 NEWS  9  AUG 18   Simultaneous left and right truncation added to ANABSTR
 NEWS 10  SEP 22   DIPPR file reloaded
 NEWS 11  SEP 25   INPADOC: Legal Status data to be reloaded
 NEWS 12  SEP 29   DISSABS now available on STN
 NEWS 13  OCT 10   PCTFULL: Two new display fields added
 NEWS 14  OCT 21   BIOSIS file reloaded and enhanced
 NEWS 15  OCT 28   BIOSIS file segment of TOXCENTER reloaded and enhanced

 NEWS EXPRESS  NOVEMBER 14 CURRENT WINDOWS VERSION IS V6.01c, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
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FILE 'HOME' ENTERED AT 10:17:24 ON 14 NOV 2003

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FILE COVERS 1907 - 14 Nov 2003 VOL 139 ISS 21
FILE LAST UPDATED: 13 Nov 2003 (20031113/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> "glycoprotein O"
         85603 "GLYCOPROTEIN"
         93770 "GLYCOPROTEINS"
        131129 "GLYCOPROTEIN"
                 ("GLYCOPROTEIN" OR "GLYCOPROTEINS")
       1388767 "O"
L1           64 "GLYCOPROTEIN O"
                 ("GLYCOPROTEIN"(W)"O")

=> CMV and L1
          5649 CMV
            49 CMVS
          5666 CMV
                 (CMV OR CMVS)
L2           3 CMV AND L1

=> "human cytomegalovirus"
       1196922 "HUMAN"
        310832 "HUMANS"
       1356656 "HUMAN"
                 ("HUMAN" OR "HUMANS")
         10297 "CYTOMEGALOVIRUS"
           129 "CYTOMEGALOVIRUSES"
         10312 "CYTOMEGALOVIRUS"
                 ("CYTOMEGALOVIRUS" OR "CYTOMEGALOVIRUSES")
L3        4184 "HUMAN CYTOMEGALOVIRUS"
                 ("HUMAN"(W)"CYTOMEGALOVIRUS")

=> L3 and l1
L4           9 L3 AND L1

=> cytomegalovirus
         10297 CYTOMEGALOVIRUS
           129 CYTOMEGALOVIRUSES
L5       10312 CYTOMEGALOVIRUS
                 (CYTOMEGALOVIRUS OR CYTOMEGALOVIRUSES)

=> L5 and l1
L6           9 L5 AND L1

=> DIS L6 1- IBIB IABS
YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):Y
THE ESTIMATED COST FOR THIS REQUEST IS 21.74 U.S. DOLLARS
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DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L6 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:408793 CAPLUS
DOCUMENT NUMBER: 138:396186
TITLE: Human **cytomegalovirus glycoprotein O** as a new drug target and subunit vaccine candidate
INVENTOR(S): Compton, Teresa; Huber, Mary T.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6569616	B1	20030527	US 2000-627986	20000728

PRIORITY APPLN. INFO.: US 1999-146180P P 19990729
ABSTRACT:
A method of designing a new anti-CMV drug is disclosed. In one embodiment, the invention comprises (a) analyzing the binding of **glycoprotein** ***O*** to a **glycoprotein O** receptor and (b) designing a candidate drug that would competitively interfere with **glycoprotein** ***O*** binding to **glycoprotein O** receptor and (c) showing that the candidate drug competitively inhibits **glycoprotein** ***O*** binding to **glycoprotein O** receptor. A method of screening anti-CMV drugs, a vaccine effective to diminish CMV infection, and a method of diminishing CMV infection are also disclosed.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:796011 CAPLUS
DOCUMENT NUMBER: 138:218045
TITLE: The genes encoding the gCIII complex of human **cytomegalovirus** exist in highly diverse combinations in clinical isolates
AUTHOR(S): Rasmussen, Lucy; Geissler, Aimee; Cowan, Catherine; Chase, Amanda; Winters, Mark
CORPORATE SOURCE: Dep. Med., Stanford Univ. Sch. Med., Stanford, CA, 94305, USA
SOURCE: Journal of Virology (2002), 76(21), 10841-10848
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The UL74 (**glycoprotein O** [gO])-UL75 (gH)-UL115 (gL) complex of human **cytomegalovirus** (CMV), known as the gCIII complex, is likely to play an important role in the life cycle of the virus. The gH and gL proteins have been assocd. with biol. activities, such as the induction of virus-neutralizing antibody, cell-virus fusion, and cell-to-cell spread of the virus. The sequences of the 2 gH gene variants, readily recognizable by restriction endonuclease polymorphism, are well conserved among clin. isolates, but nothing is known about the sequence variability of the gL and gO genes. Sequencing of the full-length gL and gO genes was performed with 22-39 clin. isolates, as well as with lab. strains AD169, Towne, and Toledo, to det. phylogenetically based variants of the genes. The sequence information provided the basis for identifying gL and gO variants by restriction endonuclease polymorphism. The predicted gL amino acid sequences varied <2%

among the isolates, but the variability of gO among the isolates approached 45%. The variants of the genes coding for gCIII in lab. strains Towne, AD169, and Toledo were different from those in most clin. isolates. When clin. isolates from different patient populations with various degrees of symptomatic CMV disease were surveyed, the gO1 variant occurred almost exclusively with the gH1 variant. The gL2 variant occurred with a significantly lower frequency in the gH1 variant group. There were no configurations of the gCIII complex that were specifically assocd. with symptomatic CMV disease or human immunodeficiency virus serol. status. The potential for the gCIII complex to exist in diverse genetic combinations in clin. isolates points to a new aspect that must be considered in studies of the significance of CMV strain variability.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:742368 CAPLUS
DOCUMENT NUMBER: 138:217971
TITLE: Expression and reconstitution of the gH/gL/gO complex of human **cytomegalovirus**
AUTHOR(S): Kinzler, Eric R.; Theiler, Regan N.; Compton, Teresa
CORPORATE SOURCE: McArdle Laboratory for Cancer Research, University of Wisconsin Medical School, Madison, WI, 53706, USA
SOURCE: Journal of Clinical Virology (2002), 25(Suppl. 2), S87-S95
CODEN: JCVIFB; ISSN: 1386-6532
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
All herpesviruses examd. to date encode a heterodimeric envelope complex consisting of glycoprotein H (gH) and glycoprotein L (gL); however, co-expression of human **cytomegalovirus** (HCMV) gH and gL is not sufficient to reconstitute the high mol. wt. complex seen in infected cells. Previously, the authors showed that HCMV encodes a third glycoprotein, gO, which assocs. with gH and gL to form an unusual tripartite complex. The objective of this study was to reconstitute the HCMV gH-contg. complex by co-expression of the gH (UL75), gL (UL115), and gO (UL74) genes. The authors co-expressed gH, gL, and gO in insect cells using a recombinant baculovirus, and in a mammalian system using triple plasmid transfection. Recombinant complexes from both systems were compared with those expressed in HCMV infected cells by SDS-PAGE and immunoblot or immunopptn. with antibodies to gH, gL, or gO. Insect cells infected with the triple gene baculovirus produced gH/gL heterodimers, gH/gL heteromultimers, and gO homomultimers, however, they did not produce detectable tripartite complex. In contrast, co-expression of gH, gL, and gO in mammalian cells produced high mol. wt. complexes that closely resemble gH/gL/gO complexes formed in HCMV infected cells. Redn. of disulfide bonds resolved high mol. wt. complexes into the three individual glycoproteins. Addnl., cell surface immunofluorescence proved that the complexes are expressed and displayed on the surface of transfected cells. Triple plasmid transfected cells produced high mol. wt. complexes that co-migrated with endogenous HCMV gH/gL/gO complexes as analyzed by SDS-PAGE. In addn., several distinct, novel forms of the three glycoproteins were detected.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:653434 CAPLUS
DOCUMENT NUMBER: 137:322360
TITLE: Membrane topology and complex formation of human **cytomegalovirus glycoprotein O**

AUTHOR(S): Theiler, Regan Nell
CORPORATE SOURCE: Univ. of Wisconsin, Madison, WI, USA
SOURCE: (2001) 181 pp. Avail.: UMI, Order No. DA3033305
From: Diss. Abstr. Int., B 2002, 62(11), 4934
DOCUMENT TYPE: Dissertation
LANGUAGE: English
ABSTRACT: Unavailable

L6 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:209906 CAPLUS
DOCUMENT NUMBER: 136:382809
TITLE: Distinct **glycoprotein O** complexes arise in a post-golgi compartment of **cytomegalovirus**-infected cells
AUTHOR(S): Theiler, Regan N.; Compton, Teresa
CORPORATE SOURCE: McArdle Laboratory for Cancer Research, University of Wisconsin-Madison Medical School, Madison, WI, 53706, USA
SOURCE: Journal of Virology (2002), 76(6), 2890-2898
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Human **cytomegalovirus** (CMV) glycoproteins H, L, and O (gH, gL, and gO, resp.) form a heterotrimeric disulfide-bonded complex that participates in the fusion of the viral envelope with the host cell membrane. During virus maturation, this complex undergoes a series of intracellular assembly and processing events which are not entirely defined. Here, we demonstrate that gO does not undergo the same posttranslational processing in transfected cells as it does in infected cells. We further detd. that gO is modified by O-linked glycosylation and that this terminally processed form is highly enriched in virions. However, during studies of gO processing, novel gO complexes were discovered in CMV virions. The newly identified gO complexes, including gO-gL heterodimers, were not readily detected in CMV-infected cells. Further characterization of the trafficking of gO through the secretory pathway of infected cells localized gH, gL, and gO primarily to the Golgi app. and trans-Golgi network, supporting the conclusion that the novel virion-assocd. gO complexes arise in a post-Golgi compartment of infected cells.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:173513 CAPLUS
DOCUMENT NUMBER: 136:366301
TITLE: A role for human **cytomegalovirus glycoprotein O** (gO) in cell fusion and a new hypervariable locus
AUTHOR(S): Paterson, David A.; Dyer, Angela P.; Milne, Richard S. B.; Sevilla-Reyes, Edgar; Gompels, Ursula A.
CORPORATE SOURCE: Pathogen Molecular Biology and Biochemistry Unit, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, University of London, London, WC1E 7HT, UK
SOURCE: Virology (2002), 293(2), 281-294
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A cell fusion assay using fusion-from-without (FFWO) recombinant adenoviruses (RAds) and specific antibody showed a role in fusion modulation for glycoprotein gO, the recently identified third component of the gH/gL gCIII

complex of human **cytomegalovirus** (HCMV). As in HCMV, RAd gO expressed multiple glycosylated species with a mature product of 125 kDa. Coexpression with gH/gL RAds showed gCIII reconstitution in the absence of other HCMV products and stabilization by intermol. disulfide bonds. Properties of HCMV clin. isolate, Pt, also implicated gO in cell spread. Compared to lab. strain AD169, Pt was resistant to gH antibody plaque inhibition, but mature gH was identical. However, the gO sequences were highly divergent (20%), with further variation in lab. strain Towne gO (34%). Thus, gO forms gCIII with gH/gL, performs in cell fusion, and is a newly identified HCMV hypervariable locus which may influence gCIII's function in mediating infection. (c) 2002 Academic Press.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:783528 CAPLUS
DOCUMENT NUMBER: 136:132673
TITLE: Characterization of the signal peptide processing and membrane association of human **cytomegalovirus glycoprotein O**
AUTHOR(S): Theiler, Regan N.; Compton, Teresa
CORPORATE SOURCE: McArdle Laboratory for Cancer Research, University of Wisconsin-Madison Medical School, Madison, WI, 53706, USA
SOURCE: Journal of Biological Chemistry (2001), 276(42), 39226-39231
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Human **cytomegalovirus** (HCMV) has a structurally complex envelope that contains multiple glycoproteins. These glycoproteins are involved in virus entry, virus maturation, and cell-cell spread of infection. Glycoprotein H (gH), glycoprotein L (gL), and **glycoprotein O** (gO) assoc. covalently to form a unique disulfide-bonded tripartite complex. ***Glycoprotein*** **O** was recently discovered, and its basic structure, as well as that of the tripartite complex, remains uncharacterized. Based on hydropathy anal., the authors hypothesized that gO could adopt a type II transmembrane orientation. The data presented here, however, reveal that the single hydrophobic domain of gO functions as a cleavable signal peptide that is absent from the mature mol. Although it lacks a membrane anchor, ***glycoprotein*** **O** is assocd. with the membranes of HCMV-infected cells. The sophisticated organization of the gH.cntdot.gL.cntdot.gO complex reflects the intricate nature of the multicomponent entry and fusion machinery encoded by HCMV.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:263435 CAPLUS
DOCUMENT NUMBER: 131:71017
TITLE: Intracellular formation and processing of the heterotrimeric gH-gL-gO (gCIII) glycoprotein envelope complex of human **cytomegalovirus**
AUTHOR(S): Huber, Mary T.; Compton, Teresa
CORPORATE SOURCE: Program in Cellular and Molecular Biology and Department of Medical Microbiology and Immunology, University of Wisconsin, Madison, WI, 53706, USA
SOURCE: Journal of Virology (1999), 73(5), 3886-3892
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The human **cytomegalovirus** (HCMV) gCIII complex contains glycoprotein H (gH;gpUL75), glycoprotein L (gL; gpUL115), and **glycoprotein** ***O*** (gO; gpUL74). To examine how gH, gL, and gO interact within HCMV-infected cells to assemble the tripartite complex, pulse-chase expts. were performed. These analyses demonstrated that gH and gL assoc. by the end of the pulse period to form a disulfide dependent gH-gL complex. Subsequently, the gH-gL complex interacts with a 100-kDa precursor form of gO to form a 220-kDa precursor of the mature gH-gL-gO complex that contains a 125-kDa form of gO. The 220-kDa precursor complex (pgCIII) was sensitive to treatment with endoglycosidase H (endo H), while the mature gCIII complex was essentially resistant to digestion with this enzyme, suggesting that formation of pgCIII complex occurs in the endoplasmic reticulum (ER) and is processed to mature gH-gL-gO (gCIII) in a post-ER compartment. While the N-linked glycans on the 100-kDa form of gO were modified to endo H-resistant states as the 125-kDa gO formed, addnl. posttranslational modifications were detected on gO. These processing alterations were non-N-linked oligosaccharide modifications that could not be accounted for by phosphorylation or by O-glycosylation of the type sensitive to O-glycanase. Of gH, gL, gO, and the various complexes that they form, only the mature form of the complex was detectable at the infected cell membrane, as judged by surface biotinylation studies.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:620269 CAPLUS
DOCUMENT NUMBER: 129:326815
TITLE: The human **cytomegalovirus** UL74 gene encodes the third component of the glycoprotein H-glycoprotein L-containing envelope complex
AUTHOR(S): Huber, Mary T.; Compton, Teresa
CORPORATE SOURCE: Program in Cellular and Molecular Biology and Department of Medical Microbiology and Immunology, University of Wisconsin-Madison, Madison, WI, 53706-1532, USA
SOURCE: Journal of Virology (1998), 72(10), 8191-8197
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The human **cytomegalovirus** (HCMV) gCIII envelope complex is composed of glycoprotein H (gH; gpUL75), glycoprotein L (gL; gpUL115), and a third, 125-kDa protein not related to gH or gL (M. T. Huber and T. Compton, J. Virol. 71:5391-5398, 1997; L. Li, J. A. Nelson, and W. J. Britt, J. Virol. 71:3090-3097, 1997). Glycosidase digestion anal. demonstrated that the 125-kDa protein was a glycoprotein contg. ca. 60 kDa of N-linked oligosaccharides on a peptide backbone of 65 kDa or less. Based on these biochem. characteristics, two HCMV open reading frames, UL74 and TRL/IRL12, were identified as candidate genes for the 125-kDa glycoprotein. To identify the gene encoding the 125-kDa glycoprotein, the authors purified the gCIII complex, sepd. the components by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, and subjected gH and the 125-kDa glycoprotein to amino acid microsequence anal. Microsequencing of an internal peptide derived from purified 125-kDa glycoprotein yielded the amino acid sequence LYVGPTK. A FASTA search revealed an exact match of this sequence to amino acids 188 to 195 of the predicted product of the candidate gene UL74, which we have designated **glycoprotein O** (gO).
Anti-gO antibodies reacted in immunoblots with a protein species migrating at ca. 100 to 125 kDa in lysates of HCMV-infected cells and with 100- and 125-kDa protein species in purified virions. Anti-gO antibodies also immunopptd. the

gCIII complex and recognized the 125-kDa glycoprotein component of the gCIII complex. Positional homologs of the UL74 gene were found in other betaherpesviruses, and comparisons of the predicted products of the UL74 homologs genes demonstrated a no. of conserved biochem. features.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> DIS L2 1- IBIB IABS
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):Y
THE ESTIMATED COST FOR THIS REQUEST IS 7.25 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L2 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:408793 CAPLUS
DOCUMENT NUMBER: 138:396186
TITLE: Human cytomegalovirus **glycoprotein O** as a new drug target and subunit vaccine candidate
INVENTOR(S): Compton, Teresa; Huber, Mary T.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6569616	B1	20030527	US 2000-627986	20000728

PRIORITY APPLN. INFO.: US 1999-146180P P 19990729
ABSTRACT:
A method of designing a new anti-**CMV** drug is disclosed. In one embodiment, the invention comprises (a) analyzing the binding of ***glycoprotein*** **O** to a **glycoprotein O** receptor and (b) designing a candidate drug that would competitively interfere with **glycoprotein O** binding to **glycoprotein** ***O*** receptor and (c) showing that the candidate drug competitively inhibits **glycoprotein O** binding to **glycoprotein** ***O*** receptor. A method of screening anti-**CMV** drugs, a vaccine effective to diminish **CMV** infection, and a method of diminishing ***CMV*** infection are also disclosed.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:796011 CAPLUS
DOCUMENT NUMBER: 138:218045
TITLE: The genes encoding the gCIII complex of human cytomegalovirus exist in highly diverse combinations in clinical isolates
AUTHOR(S): Rasmussen, Lucy; Geissler, Aimee; Cowan, Catherine; Chase, Amanda; Winters, Mark
CORPORATE SOURCE: Dep. Med., Stanford Univ. Sch. Med., Stanford, CA, 94305, USA
SOURCE: Journal of Virology (2002), 76(21), 10841-10848
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The UL74 (**glycoprotein O** [gO])-UL75 (gH)-UL115 (gL) complex

of human cytomegalovirus (**CMV**), known as the gCIII complex, is likely to play an important role in the life cycle of the virus. The gH and gL proteins have been assocd. with biol. activities, such as the induction of virus-neutralizing antibody, cell-virus fusion, and cell-to-cell spread of the virus. The sequences of the 2 gH gene variants, readily recognizable by restriction endonuclease polymorphism, are well conserved among clin. isolates, but nothing is known about the sequence variability of the gL and gO genes. Sequencing of the full-length gL and gO genes was performed with 22-39 clin. isolates, as well as with lab. strains AD169, Towne, and Toledo, to det. phylogenetically based variants of the genes. The sequence information provided the basis for identifying gL and gO variants by restriction endonuclease polymorphism. The predicted gL amino acid sequences varied <2% among the isolates, but the variability of gO among the isolates approached 45%. The variants of the genes coding for gCIII in lab. strains Towne, AD169, and Toledo were different from those in most clin. isolates. When clin. isolates from different patient populations with various degrees of symptomatic ***CMV*** disease were surveyed, the gO1 variant occurred almost exclusively with the gH1 variant. The gL2 variant occurred with a significantly lower frequency in the gH1 variant group. There were no configurations of the gCIII complex that were specifically assocd. with symptomatic **CMV** disease or human immunodeficiency virus serol. status. The potential for the gCIII complex to exist in diverse genetic combinations in clin. isolates points to a new aspect that must be considered in studies of the significance of ***CMV*** strain variability.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:209906 CAPLUS
DOCUMENT NUMBER: 136:382809
TITLE: Distinct **glycoprotein O** complexes arise in a post-golgi compartment of cytomegalovirus-infected cells
AUTHOR(S): Theiler, Regan N.; Compton, Teresa
CORPORATE SOURCE: McArdle Laboratory for Cancer Research, University of Wisconsin-Madison Medical School, Madison, WI, 53706, USA
SOURCE: Journal of Virology (2002), 76(6), 2890-2898
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Human cytomegalovirus (**CMV**) glycoproteins H, L, and O (gH, gL, and gO, resp.) form a heterotrimeric disulfide-bonded complex that participates in the fusion of the viral envelope with the host cell membrane. During virus maturation, this complex undergoes a series of intracellular assembly and processing events which are not entirely defined. Here, we demonstrate that gO does not undergo the same posttranslational processing in transfected cells as it does in infected cells. We further detd. that gO is modified by O-linked glycosylation and that this terminally processed form is highly enriched in virions. However, during studies of gO processing, novel gO complexes were discovered in **CMV** virions. The newly identified gO complexes, including gO-gL heterodimers, were not readily detected in **CMV** -infected cells. Further characterization of the trafficking of gO through the secretory pathway of infected cells localized gH, gL, and gO primarily to the Golgi app. and trans-Golgi network, supporting the conclusion that the novel virion-assocd. gO complexes arise in a post-Golgi compartment of infected cells.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> UL74 (l) CMV
             4 UL74
          5649 CMV
            49 CMVS
          5666 CMV
                 (CMV OR CMVS)
L7           1 UL74 (L) CMV

=> DIS L7 1 IBIB IABS
THE ESTIMATED COST FOR THIS REQUEST IS 2.42 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L7   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:        2002:796011  CAPLUS
DOCUMENT NUMBER:         138:218045
TITLE:                   The genes encoding the gCIII complex of human
                         cytomegalovirus exist in highly diverse combinations
                         in clinical isolates
AUTHOR(S):               Rasmussen, Lucy; Geissler, Aimee; Cowan, Catherine;
                         Chase, Amanda; Winters, Mark
CORPORATE SOURCE:        Dep. Med., Stanford Univ. Sch. Med., Stanford, CA,
                         94305, USA
SOURCE:                  Journal of Virology (2002), 76(21), 10841-10848
                         CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER:               American Society for Microbiology
DOCUMENT TYPE:           Journal
LANGUAGE:                English
ABSTRACT:
The UL74 (glycoprotein O [gO])-UL75 (gH)-UL115 (gL) complex of human
cytomegalovirus (CMV), known as the gCIII complex, is likely to play
an important role in the life cycle of the virus.  The gH and gL proteins have
been assocd. with biol. activities, such as the induction of virus-neutralizing
antibody, cell-virus fusion, and cell-to-cell spread of the virus.  The
sequences of the 2 gH gene variants, readily recognizable by restriction
endonuclease polymorphism, are well conserved among clin. isolates, but nothing
is known about the sequence variability of the gL and gO genes.  Sequencing of
the full-length gL and gO genes was performed with 22-39 clin. isolates, as
well as with lab. strains AD169, Towne, and Toledo, to det. phylogenetically
based variants of the genes.  The sequence information provided the basis for
identifying gL and gO variants by restriction endonuclease polymorphism.  The
predicted gL amino acid sequences varied <2% among the isolates, but the
variability of gO among the isolates approached 45%.  The variants of the genes
coding for gCIII in lab. strains Towne, AD169, and Toledo were different from
those in most clin. isolates.  When clin. isolates from different patient
populations with various degrees of symptomatic CMV disease were
surveyed, the gO1 variant occurred almost exclusively with the gH1 variant.
The gL2 variant occurred with a significantly lower frequency in the gH1
variant group.  There were no configurations of the gCIII complex that were
specifically assocd. with symptomatic CMV disease or human
immunodeficiency virus serol. status.  The potential for the gCIII complex to
exist in diverse genetic combinations in clin. isolates points to a new aspect
that must be considered in studies of the significance of CMV strain
variability.

REFERENCE COUNT:        54    THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> CMV (l) latent (w) infection
          5649 CMV
            49 CMVS
          5666 CMV
                 (CMV OR CMVS)
```

```
         43161 LATENT
             1 LATENTS
         43162 LATENT
                 (LATENT OR LATENTS)
        195496 INFECTION
         59197 INFECTIONS
        225416 INFECTION
                 (INFECTION OR INFECTIONS)
L8          31 CMV (L) LATENT (W) INFECTION

=> prevetion (l) CMV
             0 PREVETION
          5649 CMV
            49 CMVS
          5666 CMV
                 (CMV OR CMVS)
L9           0 PREVETION (L) CMV

=> prevention (l) CMV
        255750 PREVENTION
           109 PREVENTIONS
        255799 PREVENTION
                 (PREVENTION OR PREVENTIONS)
          5649 CMV
            49 CMVS
          5666 CMV
                 (CMV OR CMVS)
L10        103 PREVENTION (L) CMV

=> vaccine and L10
         40596 VACCINE
         41280 VACCINES
         51037 VACCINE
                 (VACCINE OR VACCINES)
L11         16 VACCINE AND L10

=> DIS L11 1- IBIB IABS
YOU HAVE REQUESTED DATA FROM 16 ANSWERS - CONTINUE? Y/(N):Y
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DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L11  ANSWER 1 OF 16  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:        2003:850676  CAPLUS
TITLE:                   Delivery of a heterologous antigen by a registered
                         Salmonella vaccine (STM1)
AUTHOR(S):               Bachtiar, Endang W.; Sheng, Kuo-Ching; Fifis,
                         Theodora; Gamvrellis, Anita; Plebanski, Magdalena;
                         Coloe, Peter J.; Smooker, Peter M.
CORPORATE SOURCE:        Department of Biotechnology and Environmental Biology,
                         RMIT University, P.O. Box 71, Bundoora, Vic, 3083,
                         Australia
SOURCE:                  FEMS Microbiology Letters (2003), 227(2), 211-217
                         CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER:               Elsevier Science B.V.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
ABSTRACT:
STM1 is an aro A- attenuated mutant of Salmonella enterica serovar Typhimurium,
and is a well-characterised vaccine strain available to the livestock
industry for the prevention of salmonellosis in chickens.  This
strain has potential for heterologous antigen delivery, and here we show that
the strain can be used to deliver a model antigen, ovalbumin, to immune cells
in vitro and in vivo.  Two plasmid constructs expressing the ovalbumin gene
were utilized, one of which uses a prokaryotic promoter and the other the
```

CMV promoter (DNA **vaccine**). In vitro, STM1 carrying ovalbumin-encoding plasmids was able to invade dendritic cells and stimulate a CD8+ cell line specific for the dominant ovalbumin epitope, SIINFEKL. In vivo, spleen cells were responsive to SIINFEKL after vaccination of mice with ovalbumin-encoding plasmids in STM1, and finally, humoral responses, including IgA, were induced after vaccination.

L11 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:705621 CAPLUS
TITLE: Assessment of DNA **vaccine** potential for gilthead sea bream (Sparus aurata) by intramuscular injection of a reporter gene
AUTHOR(S): Verri, Tiziano; Ingrosso, Laura; Chiloiro, Rita; Danieli, Antonio; Zonno, Vincenzo; Alifano, Pietro; Romano, Nicla; Scapigliati, Giuseppe; Vilella, Sebastiano; Storelli, Carlo
CORPORATE SOURCE: Department of Biological and Environmental Sciences and Technologies, University of Lecce, via Provinciale Lecce-Monteroni, Lecce, I-73100, Italy
SOURCE: Fish & Shellfish Immunology (2003), 15(4), 283-295
CODEN: FSIMEP; ISSN: 1050-4648
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Naked circular plasmid DNA contg. the cytomegalovirus (**CMV**)-promoter-driven lacZ reporter gene (pCMV-LacZ) was injected in the epaxial muscle of gilthead sea bream (Sparus aurata). A mosaic pattern of expression of .beta.-galactosidase (.beta.-gal) in the myofibres at the site of injection was visualised by in situ histochem. staining using 5-bromo-4-chloro-3-indolyl-.beta.-d-galactopyranoside. As measured by o-nitrophenyl-.beta.-d-galactopyranoside assay, .beta.-gal enzymic activity was found to steadily increase for at least 50 days post injection (p.i.) in pCMV-LacZ-injected muscle. In parallel, foreign DNA was detected by polymerase chain reaction in injected muscles (but not in other tissues) up to 60 days p.i., persisting most probably in an extrachromosomal, non-replicative, circular form. Neither .beta.-gal activity nor pCMV-LacZ-related amplification products were found 90 days p.i. Antibodies against .beta.-gal were demonstrated in pCMV-LacZ-injected fish sampled 45 days p.i. The results suggest that i.m. delivery of foreign genes represents a realistic approach for DNA ***vaccine*** technol. for the **prevention** of infectious diseases in gilthead sea bream.

L11 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:659578 CAPLUS
DOCUMENT NUMBER: 137:194894
TITLE: Prophylaxis of herpesvirus infections in immunocompetent and immunocompromised older patients
AUTHOR(S): Fillet, Anne-Marie
CORPORATE SOURCE: Virology Department, Pitie-Salpetriere Hospital AP-HP and University, Paris, Fr.
SOURCE: Drugs & Aging (2002), 19(5), 343-354
CODEN: DRAGE6; ISSN: 1170-229X
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review. In older patients, prophylaxis of herpesvirus infections mainly involves preventing the recurrence of herpes simplex virus (HSV) and complications of herpes zoster in immunocompetent patients, while in immunocompromised patients it is more concerned with the **prevention** of opportunistic virus reactivation. HSV ocular infection is the most frequent

cause of corneal blindness in the US. The effectiveness fo aciclovir 400mg twice daily in preventing the recurrence of HSV eye disease in immunocompetent patients has been well demonstrated. The issue of treatment duration for patients with highly recurrent ocular herpes remains unresolved. Post-herpetic neuralgia (PHN) is one of the most common neuralgic illnesses worldwide. Some progress in **prevention** of PHN has been made with a combination of antiviral therapy (famciclovir or valaciclovir), started within 72 h of onset of the rash, and analgesic treatment. However, the best **prevention** of PHN is the **prevention** of herpes zoster disease, and the varicella ***vaccine*** is an option which over the next few years will be tested in clin. trials. For immunocompromised patients of any age, restoring immunity prevents herpesvirus disease, as demonstrated for cytomegalovirus (**CMV**) in AIDS patients receiving highly active antiretroviral therapy. Specific antiviral therapy during the initial period after transplantation could prevent reactivation of HSV or **CMV** in seropos. recipients. Whether preemptive therapy or prophylaxis with ganciclovir is the optimal approach against **CMV** remains controversial, and the relative merits and limitations of each approach may guide the choice. In stem cell transplantation, preemptive therapy with foscarnet avoids the neutropenia and related complications assocd. with ganciclovir. In renal transplant recipients, universal prophylaxis of **CMV** infection with valaciclovir has the same efficacy as ganciclovir. Although it is relatively toxic, cidofovir should be further evaluated because of its in vitro activity against most DNA viruses.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:614269 CAPLUS
TITLE: Construction, expression, and immunologic evaluation of a multiprotein CMV **vaccine** candidate in MVA
AUTHOR(S): Diamond, Don J.; Wang, Zhongde; LaRosa, Corinna; Lacey, Simon; Villacres, Maria; Sharan, Rahul; Buck, Chris; Maas, Rebecca; Markel, Susan; Brewer, John; Mekhoubad, Shahram; Siliciano, Robert F.
CORPORATE SOURCE: Laboratory of Vaccine Research, Beckman Research Institute of the City of Hope, Duarte, CA, 91010, USA
SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), BIOT-313. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
ABSTRACT:
Reactivation of latent **CMV** among immunosuppressed patients recovering from bone marrow or solid organ transplantation leads to increased morbidity and mortality. Because of the limitations of triple drug therapy, HIV-1 patients on HAART may require a **CMV vaccine** to enhance immunity to prevent **CMV** reactivation. To address the problem of ***CMV*** reactivation and **prevention** of infection, we have used an attenuated poxvirus (MVA) to express **CMV** proteins. This viral ***vaccine*** candidate has several advantageous properties including avirulence in humans, low inflammatory response, and low vector immunogenicity. The aim of this **vaccine** is to reconstitute both humoral (gB neutralizing antibodies) and cellular (pp65, pp150, IE1) immunity to ***CMV*** , including both T-help and CTL responses. Use of full length ***CMV*** proteins should provide **vaccine** coverage for most ethnic groups, even those with rare HLA alleles. The initial goal has been the construction of a recombinant (r)MVA simultaneously expressing multiple ***CMV*** proteins, after insertion of engineered transcription units into dispensable viral DNA sites by homologous recombination. Targeting of

CMV proteins for proteasomal degrdn. has been accomplished by insertion of monomeric ubiquitin at the N-terminus of pp65, pp150, and IE1. We have shown that ubiquitin-targeting to the proteasome enhances the effectiveness of antigen presentation. An important consequence of more efficient processing is the powerful stimulation of **CMV**-specific memory CD4 and CD8 T cells by these candidate **vaccine** antigens in PBMC from healthy volunteers. We have utilized **CMV**-specific HLA-tetramers to quantitate the increased frequency of the elicited memory T cells, and functional assays to demonstrate their specificity and lytic activity. We have also conducted immunization studies in HLA-transgenic mice, including anal. of the breadth of the CTL response with **CMV**-specific HLA-tetramers. Prime-boost immunization strategies have been evaluated, including administration of the rMVA both at mucosal sites and parenterally to harness the activity of the systemic and mucosal immune systems. The goal of this project is to develop and clin. evaluate a viral **vaccine** candidate that will stimulate cellular and humoral immunity to **CMV**, as a means to suppress or prevent **CMV** reactivation and/or viremia in at-risk patients.

L11 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:249469 CAPLUS
DOCUMENT NUMBER: 137:4589
TITLE: DNA **vaccines** against cytomegalovirus: current progress
AUTHOR(S): Temperton, N. J.
CORPORATE SOURCE: Academic Centre for Travel Medicine and Vaccines, Department of Virology, Royal Free and University College Medical School, London, NW3 2PF, UK
SOURCE: International Journal of Antimicrobial Agents (2002), 19(3), 169-172
CODEN: IAAGEA; ISSN: 0924-8579
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review. The development of a **vaccine** for the **prevention** of primary cytomegalovirus (**CMV**) infection is a major public health priority. Live attenuated virus, recombinant viral vector, recombinant protein and peptide **vaccines** have been studied as potential **vaccine** candidates. In recent years, DNA vaccination strategies have been developed for many pathogens, including **CMV**. This review aims to bring together many aspects of this relatively new **vaccine** technol. as applied to current research into the development of **vaccines** against ***CMV*** .

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:243568 CAPLUS
DOCUMENT NUMBER: 137:165864
TITLE: Mechanisms of replication of alpha- and betaherpesviruses and their pathogenesis
AUTHOR(S): Rajcani, J.; Durmanova, V.
CORPORATE SOURCE: Institute of Virology, Slovak Academy of Sciences, Bratislava, Slovakia
SOURCE: Bratislavske Lekarske Listy (2001), 102(11), 505-514
CODEN: BLLIAX; ISSN: 0006-9248
PUBLISHER: Slovak Academic Press Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review. The diseases caused by herpes simplex virus (HSV) and human cytomegalovirus (**CMV**) differ and distinct differences in biol.

properties of these viruses can be noticed at lab. work. Despite this, the structure of DNA and the replication cycle of both viruses shows remarkably common features. Analogous proteins encoded by both viruses, act at initiation of viral DNA transcription, at viral DNA synthesis, at nucleocapsid formation and envelopment. On other hand, considerable differences occur during maturation of virions and at their egress from infected cells. Both viruses in question developed strategies to escape immune recognition by cytotoxic T cells and/or to interfere with the antibody response. Both viruses are widespread in the human population and are able to establish latency. Finally, their ***prevention*** and/or prophylaxis by effective **vaccines** has not been solved. Recently, the significance of both viruses has increased. HSV2 is an important pathogen acquired by sexual contact, while **CMV** reactivates under immunosuppression (post-transplantation, tumors, combined activation in the presence of human immunodeficiency virus) and/or causes congenital infection. Chemotherapy of HSV mediated diseases seems more effective than that of **CMV** mediated infection, because the ***CMV*** inhibitor ganciclovir is much more toxic than the **CMV** inhibitor acyclovir and its derivs.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:223206 CAPLUS
DOCUMENT NUMBER: 137:123752
TITLE: Effect of previous or simultaneous immunization with canarypox expressing cytomegalovirus (CMV) glycoprotein B (gB) on response to subunit gB **vaccine** plus MF59 in healthy CMV-seronegative adults
AUTHOR(S): Bernstein, David I.; Schleiss, Mark R.; Berencsi, Klara; Gonczol, Eva; Dickey, Michelle; Khoury, Phil; Cadoz, Michel; Meric, Claude; Zahradnik, John; Duliege, Anne-Marie; Plotkin, Stanley
CORPORATE SOURCE: Div of Infectious Diseases, Children's Hospital Medical Center, Cincinnati, OH, 45229-3039, USA
SOURCE: Journal of Infectious Diseases (2002), 185(5), 686-690
CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER: University of Chicago Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Development of a **vaccine** for **prevention** of congenital cytomegalovirus (**CMV**) disease is a priority. This study evaluated a "prime-boost" strategy by comparing the safety and immunogenicity of 3 doses of subunit **CMV** glycoprotein B (gB) **vaccine** plus MF59 (a squalene-in-water emulsion), 2 doses of a canarypox recombinant **vaccine** expressing CMVgB (ALVAC-CMVgB) followed by 2 doses of the subunit gB ***vaccine*** , 3 doses of both **vaccines** administered concomitantly, and placebo in 105 healthy, **CMV**-seroneg. adults. Systemic adverse events were rare, but local reactions were common in all groups. After the first subunit vaccination, neutralizing antibody titers in the prime-boost group were comparable to those in subjects receiving 2 subunit vaccinations, indicating a priming effect of ALVAC-CMVgB. However, after the final dose, antibody and cell-mediated immune responses were not significantly different among the groups. All 3 **vaccine** regimens induced high-titer antibody and lymphoproliferative responses, but no benefit for priming or simultaneous vaccination was detected.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:71063 CAPLUS

DOCUMENT NUMBER: 136:256627
TITLE: Cytomegalovirus infection in immunocompetent and immunocompromised individuals - a review
AUTHOR(S): Vancikova, Z.; Dvorak, P.
CORPORATE SOURCE: 1st Department of Paediatrics, 2nd Medical School, Charles University, Prague, 150 06/5, Czech Rep.
SOURCE: Current Drug Targets: Immune, Endocrine and Metabolic Disorders (2001), 1(2), 179-187
CODEN: CDTIBT; ISSN: 1568-0088
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review. This review summarizes the state-of-the-art knowledge on diagnosis, pathogenesis, immune response to, clin. picture, treatment and ***prevention*** of cytomegalovirus (**CMV**) infection in humans. ***CMVs*** are ubiquitous betaherpesviruses that infect animals as well as humans. Primary infection with human cytomegalovirus (HCMV) is followed by persistence of the virus in a latent form. During life, the virus can reactivate, resulting in renewed shedding of the virus or development of disease. Redundant mol. mechanisms have been identified by which **CMVs** interfere with the host immune control, but finally, the infection is held in check by the host's immune response. As a consequence, **CMV** disease is restricted to the immunocompromised or immunol. immature host. HCMV is the leading cause of congenital infections, with an incidence of 1-2,4% of live births, with possible severe classic "cytomegalovirus inclusion disease" in 10% of them. Congenital **CMV** infection is the leading infectious cause of brain damage and hearing loss in children and also a relevant health issue to transplant recipients and human immunodeficiency virus (HIV) -infected patients. Significant progress has been made in the last few years in detecting **CMV**, but in the immunocompromised patients, establishing the diagnosis of **CMV** infection can still be problematic. The most sensitive mol. amplification methods such as polymerase chain reaction (PCR) should be used. The decision how to treat the infection depends mainly on the immune status of the host. In immunocompetent patients only symptomatic treatment is recommended, while in immunocompromised patients antiviral therapy and immunotherapy should be used. The most commonly used antivirotics are: ganciclovir, foscarnet, cidofovir, valganciclovir, valaciclovir.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:878631 CAPLUS
DOCUMENT NUMBER: 137:107890
TITLE: Construction and preliminary appraisement of HSV-1 truncated gB gene DNA
AUTHOR(S): Shi, Lin; Fan, Guixiang; Yuan, Yukang; Wang, Junyang
CORPORATE SOURCE: Department of Immunology, Medical School, Xi'an Jiaotong University, Xi'an, 710061, Peop. Rep. China
SOURCE: Xi'an Yike Daxue Xuebao (2001), 22(5), 425-428, 450
CODEN: XYDXEZ; ISSN: 0258-0659
PUBLISHER: Xi'an Yike Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
ABSTRACT:
A truncated herpes simplex virus type 1 (HSV-1) glycoprotein B (gB) gene DNA ***vaccine*** was constructed for **prevention** of infection from (HSV-1). By PCR technique, a fragment of DNA sequence encoding the amino acid sequence 1-517 of the HSV-1 gB was obtained from HSV-1 genome. The fragment was then inserted into the lower stream of **CMV** promoter in the eukaryotic plasmid pcDNA 3.1 (+) mediated by intermediary vector plasmid pGEMT. The recombinant eukaryotic plasmid could correctly express the order gene and induce and immune protection against HSV-1 in vivo. This research paved the

way for study on truncated HSV-1 gB gene DNA **vaccine**, and also made the found for construction of multivalent DNA **vaccine** of HSV-1.

L11 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:466582 CAPLUS
DOCUMENT NUMBER: 136:165457
TITLE: Development of a cytomegalovirus **vaccine**: lessons from recent clinical trials
AUTHOR(S): Gonczol, Eva; Plotkin, Stanley
CORPORATE SOURCE: Wistar Institute/Albert Szent-Gyorgyi Medical University and Aventis Pasteur, Swiftwater, PA, USA
SOURCE: Expert Opinion on Biological Therapy (2001), 1(3), 401-412
CODEN: EOBTA2; ISSN: 1471-2598
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review. Cytomegalovirus-caused diseases are preventable. We believe that both neutralizing antibodies and cell-mediated immunity are necessary for ***prevention*** . Of the **CMV** proteins, gB and pp65 are the min. requirements in a **vaccine** to induce neutralizing antibodies and cytotoxic T-lymphocyte (CTL) responses. Immunization with addnl. proteins, e.g., gH, gN for neutralizing antibodies and IE1exon 4 and pp150 for CTL responses, would strengthen protective immune responses. Approaches to development of a safe and effective cytomegalovirus (**CMV**) ***vaccine*** for the **prevention** of **CMV** diseases include: a) a live attenuated **vaccine** (Towne strain); b) recombinant constructs of the attenuated Towne and the virulent Toledo **CMV** strains; c) subunit glycoprotein B (gB) adjuvanted with MF59 to induce neutralizing antibodies; d) phosphoprotein 65 (pp65) peptide-based ***vaccines*** to induce (CTL) for use in therapeutic vaccination; e) canarypox-**CMV** recombinants, e.g., ALVAC-**CMV**(gB) and ALVAC-***CMV*** (pp65) to induce neutralizing antibodies and CTL responses, resp.; f) DNA plasmids contg. the genes for gB and pp65; g) dense bodies contg. the key antigens. The attenuated Towne strain, gB/MF59, ALVAC-**CMV**(gB) and ALVAC-**CMV**(pp65) approaches have already been tested in clin. trials. The Towne **vaccine** induced neutralizing antibodies and cell-mediated immunity (including CTLs) mitigated **CMV** disease in seroneg. renal transplant recipients and protected against a low-dose virulent ***CMV*** challenge in normal volunteers but did not prevent infection in mothers of children excreting **CMV**. Immunization with gB/MF59 resulted in high levels of neutralizing antibodies in seroneg. subjects. ALVAC-**CMV**(gB) did not induce neutralizing antibodies but primed the immune system to a Towne strain challenge, while ALVAC-**CMV**(pp65) induced long-lasting CTL responses in all originally seroneg. volunteers, with CTL precursor frequency similar to naturally seropos. individuals. These results suggest that **CMV** diseases can be prevented or attenuated and that a **vaccine** combining ALVAC-**CMV**(pp65) with gB/MF59 may induce sufficient CTLs and neutralizing antibodies to protect against ***CMV*** diseases. Meanwhile, other approaches such as DNA peptide and dense body **vaccines**, should enter Phase I trials. All candidate ***vaccines*** will have to demonstrate that immunogenicity provides protection. Combined **vaccines** contg. canarypox (ALVAC) vectors to express **CMV**-pp65 to induce CTLs and of subunit gB, given together with an appropriate adjuvant to induce neutralizing antibodies, should be tested in a target population for the **prevention** of **CMV** infection and disease.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:264425 CAPLUS
DOCUMENT NUMBER: 132:273708
TITLE: Current management strategies for the treatment and prevention of cytomegalovirus infection in solid organ transplant recipients
AUTHOR(S): Abu-Nader, Rima; Patel, Robin
CORPORATE SOURCE: Division of Infectious Diseases and Department of Internal Medicine, Mayo Clinic and Foundation, Rochester, MN, USA
SOURCE: BioDrugs (2000), 13(3), 159-175
CODEN: BIDRF4; ISSN: 1173-8804
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review with 198 refs. Cytomegalovirus (**CMV**) infection in solid organ transplantation is assocd. with significant morbidity and mortality. Primary infection, secondary infection or superinfection may occur in this setting. Progression to disease may ensue with development of symptoms, with or without organ involvement. The mainstay of treatment of **CMV** disease is i.v. ganciclovir. Aside from protective organ matching and use of ***CMV*** -seroneg. blood products, methods of preventing **CMV** infection and disease include passive immunization with Igs, vaccination, and prophylaxis with antiviral agents such as aciclovir, oral or i.v. ganciclovir, and oral valaciclovir. A promising subunit **vaccine** is currently being investigated. Preemptive therapy is a form of **prevention** that is based either on the early detection of **CMV** or targeting of transplant recipients with risk factors for **CMV**. New sensitive lab. assays, including the pp65 antigenemia assay, qual., quant. and reverse-transcription polymerase chain reaction assays, hybridization assays, and nucleic acid sequence-based assays, have the ability to detect early ***CMV*** replication before disease becomes evident. These assays are being used as prospective surveillance tests, with pre-emptive therapy initiated when they become pos. or demonstrate an increasing titer.

REFERENCE COUNT: 198 THERE ARE 198 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:369851 CAPLUS
DOCUMENT NUMBER: 131:166055
TITLE: Molecular characterization of the guinea-pig cytomegalovirus glycoprotein L gene
AUTHOR(S): Paglino, J. C.; Brady, R. C.; Schleiss, M. R.
CORPORATE SOURCE: Division of Infectious Diseases, Children's Hospital Research Foundation, Cincinnati, OH, USA
SOURCE: Archives of Virology (1999), 144(3), 447-462
CODEN: ARVIDF; ISSN: 0304-8608
PUBLISHER: Springer-Verlag Wien
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Although the guinea pig cytomegalovirus (GPCMV) model is well suited to the study of **vaccines** for **prevention** of congenital **CMV** infection, there has been limited mol. characterization of GPCMV glycoproteins. Since the in vivo co-expression of the human cytomegalovirus (HCMV) glycoprotein H (gH, gpUL75) with glycoprotein L (gL, gpUL115) may have relevance to **CMV vaccine** studies, these expts. were undertaken to test whether the GPCMV encodes a gL homolog. Sequencing of the EcoR I "G" fragment of the GPCMV genome identified an open reading frame (ORF) of 774 nucleotides capable of encoding a protein of 258 amino acids. Computer matrix analyses demonstrated identity between this ORF and the gL coding sequences of other betaherpesviruses. Sequence anal. also identified an ORF

with identity to the HCMV uracil DNA glycosylase (UDG, UL114 gene). The GPCMV gL ORF encodes 6 cysteine residues, contains 3 potential N-linked glycosylation sites, and has a predicted Mr of 29.7 kDa. Northern blot studies identified an abundant 2.7 kb "early" transcript from infected cells, the putative gL message. In vitro translation of gL mRNA in reticulocyte lysate resulted in synthesis of 30 kDa polypeptide. A polyclonal antiserum was raised against a gL/glutathione-S-transferase fusion protein generated in E. coli using the pGEX expression system. This antibody identified a 40-kDa virion-assocd. protein, the putative GPCMV gL, in immunoblot assays.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:292972 CAPLUS
DOCUMENT NUMBER: 131:126069
TITLE: Construction of adenovirus 4 vector with deletion of 78.9-86 mu fragment and express of .beta.-galactosidase gene
AUTHOR(S): Shi, Changxin; Liu, Shuqiang; Zhou, Wei; Wen, Leying; Jiang, Guoqiao; Wang, Zhan; Hong, Tao
CORPORATE SOURCE: Institute of Virology, Chinese Academy of Preventive Medicine, Beijing, 100052, Peop. Rep. China
SOURCE: Zhonghua Shiyan He Linchuang Bingduxue Zazhi (1999), 13(1), 20-22
CODEN: ZSLZFS; ISSN: 1003-9279
PUBLISHER: Zhonghua Shiyan He Linchuang Bingduxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
ABSTRACT:
Adenovirus 4 (Ad4) DNA was extd. from purified virus cultured in WI-38 cells to construct a human adenovirus type 4 (Ad4) vector with partial deletions at the E3 region (78.9-86 mu). The essential fragment (71.3-100 mu) covering Ad4 E3 region was cloned and partial deletion of E3 region of this clone has been performed, generating plasmid pAd4.gamma.KS. A .beta.-galactosidase (.beta.-gal) gene flanked by **CMV** early promoter and SV40 polyA signal was inserted into pAd4.gamma.KS, resulting in pAd4c.beta.. This plasmid was cotransfected with Ad4 DNA, BclI A fragments into 293 cells, producing a non-defective recombinant Ad4 virus encoding B-gal. The constructed recombinant virus could efficiently express the foreign gene for .beta.-gal. Ad4 vector with a deletion of E3 region can be explored as a live ***vaccine*** for **prevention** of human infectious diseases. with a deletion of E3 region can be explored as a live **vaccine** for the ***prevention*** of human infection diseases.

L11 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:797199 CAPLUS
DOCUMENT NUMBER: 130:135339
TITLE: Viral satellite RNAs for the **prevention** of cucumber mosaic virus (**CMV**) disease in field-grown pepper and melon plants
AUTHOR(S): Montasser, M. S.; Tousignant, M. E.; Kaper, J. M.
CORPORATE SOURCE: Department of Biological Sciences, Faculty of Science, University of Kuwait, Safat, 13060, Kuwait
SOURCE: Plant Disease (1998), 82(12), 1298-1303
CODEN: PLDIDE; ISSN: 0191-2917
PUBLISHER: American Phytopathological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A benign viral satellite RNA, in combination with a mild strain of cucumber mosaic virus (CMV-S), was used as a "**vaccine**" or "preinoculum" to demonstrate the feasibility of protecting pepper (Capsicum annuum cv.

California Wonder) and melon (Cucurbita melo cv. Janus des Canaries) against two severe CMV strains, CMV-D and CMV-16, in the final 2 yr of a 4-yr pilot field and greenhouse expt. In the field, healthy pepper and melon seedlings challenged with CMV-D and CMV-16 showed reduced yields by 33 to 60%; CMV-S caused only limited yield redn. in pepper and had no effect on the yield of melon. Different time intervals between preinoculation of pepper and melon seedlings with CMV-S and challenge inoculation with the severe CMV strains were tested. All plants challenged 3 wk after vaccination showed nearly complete protection from subsequent infection by severe strains. The yield from preinoculated and challenged pepper plants was 80% that of untreated plants, while the yield from preinoculated and challenged melon plants was increased slightly over the untreated control plants. The use of this technol. for biol. control of plant viruses is discussed.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:542976 CAPLUS
DOCUMENT NUMBER: 129:160622
TITLE: Restenosis/atherosclerosis diagnosis, prophylaxis and therapy
INVENTOR(S): Epstein, Stephen E.; Finkel, Toren; Speir, Edith; Zhou, Yi Fu; Zhu, Jianhui; Erdile, Lorne; Pincus, Steven
PATENT ASSIGNEE(S): Pasteur Merieux Serums Et Vaccins, Fr.; Department of Health & Human Services, United States of America
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9833510	A1	19980806	WO 1998-US2191	19980205
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6183752	B1	20010206	US 1997-796101	19970205
EP 973536	A1	20000126	EP 1998-906152	19980205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-796101 A 19970205
WO 1998-US2191 W 19980205

ABSTRACT:
Disclosed and claimed are compns. and methods for therapy and/or ***prevention*** of restenosis and/or atherosclerosis. The compns. can include an agent for decreasing viral load of cytomegalovirus, such as an immunol. compn. or **vaccine** against cytomegalovirus (**CMV**) contg. at least one epitope of interest of **CMV** and/or an expression system which expresses at least one epitope of interest of **CMV**. Such compns. can include at least one epitope of p53. Alternatively, the compns. can include at least one epitope of p53 and/or an expression system which expresses the epitope. The methods can include administering the compns. to a patient in need of such therapy and/or **prevention**. Addnl., compns. and methods for diagnosing atherosclerosis and/or restenosis, or susceptibility thereto, including screening a sample from a patient for antibodies to ***CMV*** and/or **CMV** proteins and/or screening a sample from a patient for specific viral proteins that predict whether the virus has been reactivated and/or antibodies thereto and/or detecting whether **CMV** nucleic acid, e.g., mRNA is present in peripheral blood monocytes (PBMCs) and/or detecting a cellular-mediated immune response to **CMV** peptides or proteins is present and/or HLA phenotyping and/or HLA genotyping.

Embodiments can include a skin test.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:92637 CAPLUS
DOCUMENT NUMBER: 126:153498
TITLE: Identification and characterization of the guinea pig cytomegalovirus glycoprotein H gene
AUTHOR(S): Brady, R. C.; Schleiss, M. R.
CORPORATE SOURCE: Division of Infectious Diseases, Children's Hospital Research Foundation, Cincinnati, OH, USA
SOURCE: Archives of Virology (1996), 141(12), 2409-2424
CODEN: ARVIDF; ISSN: 0304-8608
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Subunit **vaccines** which target viral envelope glycoproteins offer promise for the **prevention** of congenital cytomegalovirus (**CMV**) infection. The guinea pig model of **CMV** infection is uniquely well suited to testing **vaccines** for **prevention** of congenital infection, since, in contrast to other animal cytomegaloviruses, the guinea pig ***CMV*** (GPCMV) crosses the placenta, producing intrauterine infection. Antibody to the **CMV** glycoproteins B (gB) and H (gH) appears to be important in conferring protective immunity. Unfortunately, little is known about specific GPCMV envelope glycoproteins. Sequencing of GPCMV genome fragments was therefore undertaken to test whether GPCMV encodes a gH homolog. Partial sequencing of the Hind III A fragment of the GPCMV genome revealed an open reading frame of 2 169 nucleotides capable of encoding a protein of 723 amino acids. Computer matrix analyses demonstrated identity between this ORF and the gH coding sequences of other herpesviruses. The GPCMV gH ORF encodes 12 highly conserved cysteine residues, contains 9 potential N-linked glycosylation sites, and has a predicted Mr of 81.6 kDa. Northern blot hybridizations with gH-specific probes identified an abundant 5.1 kb mRNA with expression kinetics of an "early" gene. A polyclonal antiserum raised against a synthetic peptide derived from the deduced amino acid sequence of the gH ORF identified a virion-assocd. protein with an approx. Mr of 85-kDa, the putative GPCMV gH, in immunoblot assays.

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THE ESTIMATED COST FOR THIS REQUEST IS 74.87 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L8 ANSWER 1 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:171825 CAPLUS
DOCUMENT NUMBER: 138:332663
TITLE: Cloning and characterization of the Pseudorabies virus latency-associated transcript promoter
AUTHOR(S): Ou, Chia-Jen; Chen, Ya-Hui; Huang, Chienjin
CORPORATE SOURCE: Department of Veterinary Medicine, National Chung-Hsing University, Taichung, Taiwan, Peop. Rep. China
SOURCE: Taiwan Shouyixue Zazhi (2002), 28(4), 252-259
CODEN: TSZAAK; ISSN: 1682-6485
PUBLISHER: Chinese Society of Veterinary Science
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Pseudorabies virus (PRV) is a neurotropic herpesvirus which can establish a

latent **infection** in the trigeminal ganglionic neurons of swine. During the **latent infection**, only one small region of the viral genome is transcriptionally active. This single transcript, designated the latency-assocd. transcript (LAT), has been recognized to play an indispensable role in establishing the latency. The purpose of this study was to directly analyze the nucleic acid sequences of LAT promoter (LAP) and to characterize its transcriptional activity in neural and nonneural cells. The PRV (TNL strain) LAT promoter was cloned by a polymerase chain reaction (PCR) cloning technique and its identity was confirmed by Southern blot hybridization and DNA sequencing. According to the nucleic acid sequences of LAP, there was a highly conserved region of 93 % homol. between the TNL strain and the American Ka strain. For further investigation of the regulation of the LAT promoter in neural cells as well as nonneural cell, three recombinant LacZ reporter plasmids under the control of the LAT, SV40 promoter, or **CMV** promoter were constructed. All of these recombinant reporter plasmids were transfected into the neural cell (neuro-2A) or the nonneural cell (LM cell), resp., and the effects of the various promoters on the transcriptional regulation of cellular species were compared. The expression of .beta.-galatosidase in each cell lysates was analyzed by std. .beta.-gal assay. The results demonstrated that the activity of the LAT promoter was higher in neuro-2A cells than in the LM cell. However, the SV40 and **CMV** promoters showed no significant differences in activity between the two cell lines. This observation suggested that the DNA sequences on the LAT promoter were pos. regulated by neural cell factors and might play an important role in PRV **latent infection** in the neural cell.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:805246 CAPLUS
DOCUMENT NUMBER: 137:277764
TITLE: Latent cytomegalovirus down-regulates major histocompatibility complex class II expression on myeloid progenitors
AUTHOR(S): Slobedman, Barry; Mocarski, Edward S.; Arvin, Ann M.; Mellins, Elizabeth D.; Abendroth, Allison
CORPORATE SOURCE: Center for Virus Research, Westmead Millennium Institute and University of Sydney, Westmead, Australia
SOURCE: Blood (2002), 100(8), 2867-2873
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Following primary infection, human cytomegalovirus (**CMV**) establishes a lifelong **latent infection** in bone marrow-derived myeloid lineage cells. Although down-modulation of major histocompatibility complex (MHC) class I and class II protein levels occurs during active viral replication, little is known about the modulation of these proteins during ***latent*** **infection**. When analyzed by flow cytometry, latently infected adherent cells collected from granulocyte macrophage progenitor (GM-P) cultures exhibited a striking redn. in MHC class II antigen present on the cell surface starting very early after exposure to virus that continued for more than 2 wk. In comparison, cell surface levels of the monocyte cell surface marker CD14 remained unaltered in these cells. A recombinant virus (RV798) lacking the virus genes US2-US11 retained the ability to downmodulate MHC class II levels during **latent infection**. Immunoblot and immunofluorescent antibody staining analyses showed that the redn. in MHC class II surface levels during latency was assocd. with a block in protein trafficking. HLA-DR was retained within cytoplasmic vesicles that also contained HLA-DM. Thus, downmodulation remained independent of all previously characterized MHC class I and class II immunomodulatory viral gene products and

involved a mechanism not previously ascribed to any viral function. These data show that **latent infection** is accompanied by reduced cell surface expression of MHC class II proteins, a strategy that would afford the virus escape from immunosurveillance and increase the chances for lifelong ***latent*** **infection**.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:742363 CAPLUS
DOCUMENT NUMBER: 138:135218
TITLE: Mouse models of cytomegalovirus latency: overview
AUTHOR(S): Reddehase, Matthias J.; Podlech, Jurgen; Grzimek, Natascha K. A.
CORPORATE SOURCE: Institute for Virology, Johannes Gutenberg-University, Mainz, 55101, Germany
SOURCE: Journal of Clinical Virology (2002), 25(Suppl. 2), S23-S36
CODEN: JCVIFB; ISSN: 1386-6532
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review. The mol. regulation of viral latency and reactivation is a central unsolved issue in the understanding of cytomegalovirus (**CMV**) biol. Like human **CMV** (hCMV), murine **CMV** (mCMV) can establish a ***latent*** **infection** in cells of the myeloid lineage. Since mCMV genome remains present in various organs after its clearance from hematopoietic cells first in bone marrow and much later in blood, there must exist one or more widely distributed cell type(s) representing the cellular site(s) of enduring mCMV latency in host tissues. Endothelial cells and histiocytes are candidates, but the question is not yet settled. Another long debated problem appears to be solved: mCMV establishes true mol. latency rather than a low-level persistence of productive infection. This conclusion is based on two recent advances. First, on a highly improved assay of infectivity, and second, on very sensitive RT-PCRs for detecting viral transcripts during latency. In essence, infectious virus and productive cycle transcripts, such as transcripts of early-phase gene M55 (gB) and ie3 transcripts specifying the essential transactivator protein IE3, were found to be absent during mCMV latency in the lungs. We will here review recent data on the variegated expression of IE-phase genes ie1 and ie2 during mCMV latency in the lungs, and on the expression patterns found in transcriptional foci during induced reactivation. We will discuss immunol. implications of ie1 gene expression during latency and will speculate a bit on how CD8 T cells might trigger latency-assocd. ie1 gene expression [illegible]t.

'ERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS
CORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RIGHT 2003 ACS on STN
519 CAPLUS
30
:ion of latent cytomegalovirus infection in
:in cells detected after transfer to brain
tures
Yoshihiro; Kawasaki, Hideya; Kosugi, Isao
partment of Pathology, Hamamatsu University
Medicine, Hamamatsu, 431-3192, Japan
E Virology (2002), 76(14), 7247-7254
/IAM; ISSN: 0022-538X
Society for Microbiology

ABSTRACT:
Cytomegalovirus (**CMV**) is the most significant infectious cause of brain disorders in humans involving the developing brain. It is hypothesized that the brain disorders occur after recurrent reactivation of the ***latent*** **infection** in some kinds of cells in the brains. In order to test this hypothesis, we examd. the reactivation of latent murine ***CMV*** (MCMV) infection in the mouse brain by transfer to brain slice culture. We infected neonatal and young adult mice intracerebrally with recombinant MCMV in which the lacZ gene was inserted into a late gene. The brains were removed 6 mo after infection and used to prep. brain slices that were then cultured for up to 4 wk. Reactivation of **latent** ***infection*** in the brains was detected by .beta.-galactosidase (.beta.-Gal) staining to assess .beta.-galactosidase expression. Viral replication was also confirmed by the plaque assay. Reactivation was obsd. in about 75% of the mice infected during the neonatal period 6 mo after infection. Unexpectedly, reactivation was also obsd. in 75% of mice infected as young adults, although the infection ratio in the brain slices was significantly lower than that in neonatally infected mice. .beta.-Gal-pos. cells were obsd. in marginal regions of the brains or immature neural cells in the ventricular walls. Immunohistochem. staining showed that the .beta.-Gal-pos. reactivated cells were neural stem or progenitor cells. These results suggest that brain disorders may occur long after infection by reactivation of **latent** ***infection*** in the immature neural cells in the brain.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:458518 CAPLUS
DOCUMENT NUMBER: 137:138959
TITLE: Enhanced protection against HSV lethal challenges in mice by immunization with a combined HSV-1 glycoprotein B:H:L gene DNAs
AUTHOR(S): Cha, Soung Chul; Kim, Young Sik; Cho, Jae Kyung; Cho, Jun; Kim, Su Yung; Kang, Hyun; Cho, Myung Hwan; Lee, Hyung Hoan
CORPORATE SOURCE: Department of Biological Sciences, Konkuk University, Seoul, 143-701, S. Korea
SOURCE: Virus Research (2002), 86(1-2), 21-31
CODEN: VIREDF; ISSN: 0168-1702
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The effectiveness of a cocktailed HSV-1 three-glycoprotein B, H, and L gene vaccine in comparison to individual glycoprotein gene vaccines was studied with regard to protecting against the HSV-1 infection. Three glycoprotein gene recombinant DNA vaccines, which produced the corresponding glycoproteins in Vero cells, were constructed using a **CMV** promoter. The cocktailed DNA vaccines were prepd. by combining all three genes. The titers of neutralizing antibody following the immunization of the five vaccines were KOS(1/1024)>B:H:L=B(1/512)>H:L(1/64)>H(1/16) genes. The mice, which were immunized with L gene alone failed to induce enough neutralizing antibody. The CTL activity was rated as KOS (95%)>B:H:L (80%)>B(60%)>H:L(50%)> H (35%) gene vaccines at an E:T ratio of 50:1. The H gene alone or L gene vaccine alone induced little CTL activity. The protection rates of the DNA-vaccinated mice against the lethal i.p. or i.m challenges were shown as KOS>B:H:L>B>H:L>H gene vaccines, and the protection activity depended on the lethal dosage of the challenging virus, which are inversely proportional to each other. Compared with the mice, which were vaccinated with individual DNA vaccines, the mice, which were vaccinated with the cocktailed three-gene vaccine, were shown to be better protected against the lethal challenging doses. It can be concluded that vaccination with the cocktailed three gene vaccines is more effective in protecting mice from the viral challenge and the protection rate varies

inversely with the amt. of lethal challenging dose used, although all DNA vaccines failed to block the **latent infection** in sensory nerves.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:395275 CAPLUS
DOCUMENT NUMBER: 137:122320
TITLE: Limited movement of Cucumber mosaic virus (CMV) in yellow passion flower in Brazil
AUTHOR(S): Gioria, R.; Espinha, L. M.; Rezende, J. A. M.; Gaspar, J. O.; Kitajima, E. W.
CORPORATE SOURCE: Department of Entomologia, Fitopatologia and Zoologia Agricola, ESALQ, USP, Piracicaba, SP13418-900, Brazil
SOURCE: Plant Pathology (2002), 51(2), 127-133
CODEN: PLPAAD; ISSN: 0032-0862
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Symptoms of Cucumber mosaic virus (**CMV**) on yellow passion flower (Passiflora edulis f. flavicarpa) are characterized by bright yellow mottling on leaves, starting at random points on the vine and diminishing in intensity towards the tip, which becomes symptomless as it grows. To det. whether symptomless portions of vines are **CMV**-free or represent ***latent*** **infection**, leaves with and without symptoms were collected from infected vines in the field. Biol., serol. (plate-trapped antigen ELISA, PTA-ELISA), Western blot and dot-blot hybridization assays showed that portions of the vines without symptoms were **CMV**-free. Vegetatively propagated vines with symptoms showed remission of symptoms on newly developed leaves. One year later, no **CMV** was detected in the upper leaves of these plants. Mech. inoculated passion flower seedlings behaved similarly; symptoms were shown by few leaves after inoculation. Afterwards, plants became symptomless and **CMV** was not detected in the upper leaves or root system, 40 or 85 days after inoculation. The mechanism responsible for remission of symptoms accompanied by **CMV** disappearance is not known.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:333880 CAPLUS
TITLE: Activation of cytomegalovirus in pig-to-primate organ xenotransplantation
AUTHOR(S): Mueller, Nicolas J.; Barth, Rolf N.; Yamamoto, Shin; Kitamura, Hiroshi; Patience, Clive; Yamada, Kazuhiko; Cooper, David K. C.; Sachs, David H.; Kaur, Amitinder; Fishman, Jay A.
CORPORATE SOURCE: Infectious Diseases Division, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Journal of Virology (2002), 76(10), 4734-4740
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Xenotransplantation of porcine organs carries the risk of reactivation of latent virus in donor and recipient tissues as well as transmission of viruses between species. We have investigated the activation of baboon cytomegalovirus (BCMV) and porcine **CMV** (PCMV) in a pig-to-primate model of

xenotransplantation. Tissues originating from a series of six swine-to-baboon composite thymokidney xenotransplants were investigated. Four immunosuppressed baboons died (survival range, 7 to 27 days) with the graft in situ. Increases in BCMV DNA copy nos. occurred in three (75%) of these baboons and was thought to be responsible for pneumonitis and the death of one animal. In two baboons, disseminated intravascular coagulation was successfully treated by graftectomy and discontinuation of immunosuppression. PCMV was upregulated in five of six xenografts (83%). PCMV infection was assocd. with ureteric necrosis in one xenograft. Although significantly increased in native tissues, low levels of BCMV and PCMV were also detected in tissues other than that of the native viral host species. The cross-species presence of **CMV** did not appear to cause clin. or histol. signs of invasive disease. Thus, viral infections with clin. disease were restricted to tissues of the native species of each virus. Intensive immune suppression currently required for xenotransplantation results in a significant risk of reactivation of **latent infections** by BCMV and PCMV. It is not yet know whether viral DNA detected across species lines represents cellular microchimerism, ongoing viral infection, or uptake of free virus. The observation of graft injury by PCMV demonstrates that ***CMV*** will be an important pathogen in immunosuppressed xenograft recipients. Strategies must be developed to exclude **CMV** from porcine organ donors.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:875760 CAPLUS
DOCUMENT NUMBER: 135:356383
TITLE: New biological defense function of macrophages. NO acts strongly as a "positive factor" at early stage of acute infection
AUTHOR(S): Noda, Satoshi; Tanaka, Kazuo; Koga, Yasuhiro
CORPORATE SOURCE: Sch. Med., Tokai Univ., Japan
SOURCE: Kagaku to Seibutsu (2001), 39(11), 702-705
CODEN: KASEAA; ISSN: 0453-073X
PUBLISHER: Gakkai Shuppan Senta
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
ABSTRACT:
A review with refs., on the pathol. of cytomegalovirus (**CMV**) infection, roles of nitric oxide (NO) in **CMV** reactivation, high susceptibility to murine **CMV** (MCMV) infection of NO synthase type 2-deficient mice, intrinsic antiviral activity of macrophages mediated by NO, and prevention of MCMV **latent infection** by NO-mediated antiviral activity of macrophages.

L8 ANSWER 9 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:678211 CAPLUS
DOCUMENT NUMBER: 136:277571
TITLE: Role of nitric oxide in murine cytomegalovirus (MCMV) infection
AUTHOR(S): Tanaka, K.; Noda, S.
CORPORATE SOURCE: Department of Infectious Diseases, Tokai University School of Medicine, Kanagawa, 259-1193, Japan
SOURCE: Histology and Histopathology (2001), 16(3), 937-944
CODEN: HIHIES; ISSN: 0213-3911
PUBLISHER: Histology and Histopathology
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review. Cytomegalovirus (**CMV**) is a typical pathogen of an opportunistic infection. In this review article, various roles of nitric oxide (NO) in murine **CMV** (MCMV) infections, including acute, persistent and

latent **infections**, are discussed. In the acute phase of MCMV infection, NO plays a protective role against MCMV infection. In contrast, NO has been proven to act as a pathogenic factor in a model of MCMV pneumonitis. In MCMV persistent infection, when MCMV was detected only in the salivary gland, T cells of mice were modified to produce a massive amt. of such cytokines as TNF-.alpha. and IFN-.gamma. upon in vivo stimulation with anti-CD3. These cytokines then induced mRNA for inducible NO synthase (iNOS), thus resulting in the prodn. of a large amt. of NO. A histochem. study demonstrated that NO damaged bronchial epithelial cells, and thereby apparently inducing pneumonitis. In the case of a **latent infection**, when viral DNA was detected in the host in spite of the absence of any infectious particle, NO increased the amt. of persistently-infected MCMV-DNA. As a result, NO was found to act as "a double edged sword" in the **CMV** -host relationship.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:205083 CAPLUS
DOCUMENT NUMBER: 134:352156
TITLE: Enrichment of immediate-early 1 (m123/pp89) peptide-specific CD8 T cells in a pulmonary CD62Llo memory-effector cell pool during latent murine cytomegalovirus infection of the lungs
AUTHOR(S): Holtappels, Rafaela; Pahl-Seibert, Marcus-Folker; Thomas, Doris; Reddehase, Matthias J.
CORPORATE SOURCE: Institute for Virology, Johannes Gutenberg University, Mainz, 55101, Germany
SOURCE: Journal of Virology (2000), 74(24), 11495-11503 CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Interstitial cytomegalovirus (**CMV**) pneumonia is a clin. relevant complication in recipients of bone marrow transplantation (BMT). Recent data for a model of exptl. syngeneic BMT and concomitant infection of BALB/c mice with murine **CMV** (mCMV) have documented the persistence of tissue-resident CD8 T cells after clearance of productive infection of the lungs. It was proposed that these cells represent antiviral "standby" memory cells whose functional role might be to help prevent reactivation of latent virus. The pool of pulmonary CD8 T cells was composed of two subsets defined by the T-cell activation marker L-selectin (CD62L): a CD62Lhi subset of quiescent memory cells, and a CD62Llo subset of recently resensitized memory-effector cells. In this study, the authors have continued this line of investigation by quantitating CD8 T cells specific for the three currently published antigenic peptides of mCMV: peptide YPHFMPTNL processed from the immediate-early protein IE1 (pp89), and peptides YGPSLYRRF and AYAGLFTPL, derived from the early proteins m04 (gp34) and M84 (p65), resp. IE1-specific CD8 T cells dominated in acute-phase pulmonary infiltrates and were selectively enriched in latently infected lungs. Notably, most IE1-specific CD8 T cells were found to belong to the CD62Llo subset representing memory-effector cells. This finding is in accordance with the interpretation that IE1-specific CD8 T cells are frequently resensitized during **latent infection** of the lungs and may thus be involved in the maintenance of mCMV latency.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:803952 CAPLUS
DOCUMENT NUMBER: 132:289504
TITLE: Delayed expression of adeno-associated virus vector

DNA
AUTHOR(S): Afione, Sandra A.; Wang, Jianming; Walsh, Scott; Guggino, William B.; Flotte, Terence R.
CORPORATE SOURCE: Departments of Physiology and Pediatrics, Johns Hopkins University, Baltimore, MD, USA
SOURCE: Intervirology (1999), 42(4), 213-220
CODEN: IVRYAK; ISSN: 0300-5526
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Two previous reports indicated that recombinant adeno-assocd. virus (rAAV) vectors were dependent on helper adenovirus (Ad) for efficient conversion of single-stranded (ss) rAAV DNA to the double-stranded (ds) form. This finding is somewhat paradoxical, however, since during a **latent** ***infection*** wild-type (wt)-AAV is rapidly converted to a ds form in the absence of Ad. Our hypothesis was that the effect obsd. in the previous studies was due to kinetic factors, i.e. to a relative delay in conversion to ds-DNA rather than to an abs. requirement for Ad. To test this, Hela cells were infected with a rAAV-**CMV**-green fluorescent protein (GFP) vector either in the presence or absence of Ad. Within the first 2 days, Ad infection resulted in a 4-fold increase in AAV vector expression and an augmentation of conversion to a ds-AAV DNA. By 6 days, however, the total no. of GFP-expressing cells in the Ad-free culture had exceeded the original no. in the Ad co-infected cells, and the conversion to ds-DNA episomes was substantial and ongoing.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:77232 CAPLUS
TITLE: In vivo disturbance of hematopoiesis in mice persistently infected with murine cytomegalovirus: impairment of stromal cell function
AUTHOR(S): Mori, Takehiko; Nakamura, Masato; Shimizu, Keiko; Ikeda, Yasuo; Ando, Kiyoshi
CORPORATE SOURCE: Division of Hematology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan
SOURCE: Virology (1999), 253(2), 145-154
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Although the pathogenic effects of a primary cytomegalovirus (**CMV**) infection on hematopoiesis has been largely investigated so far, the effects of a persistent or **latent infection** have yet to be elucidated. The effects of persistent **CMV** infection on hematopoiesis thus were examd. using BALB/c mice at 4 wk postinfection with 0.2 LD50 of murine ***CMV*** (MCMV) infection as a persistent infection model. The parameters of constitutive hematopoiesis of MCMV persistently infected mice were completely identical to those of the control. However, the inductive hematopoiesis, examd. by the autologous marrow reconstitution after 5-fluorouracil administration, was significantly impaired in the MCMV persistently infected mice ($P < 0.05$). In a colony-forming unit-spleen assay and a long-term bone marrow culture system, a decreased capacity of bone marrow stromal cells to support hematopoiesis was obsd. in the MCMV-infected mice in comparison with the controls. The existence of MCMV DNA in the adherent cells of long-term bone marrow culture from the MCMV-infected mice were confirmed by a polymerase chain reaction but not in the nonadherent cells. Furthermore, the increased expression level of tumor necrosis factor-.alpha. by stromal cells was also obsd. by semiquant. reverse transcriptase-polymerase chain reaction.

These results therefore strongly suggest that MCMV remains to infect the stromal cells while also inhibiting inductive hematopoiesis through the impairment of the stromal cell functions in the MCMV persistently infected mice. (c) 1999 Academic Press.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:255754 CAPLUS
DOCUMENT NUMBER: 129:36872
TITLE: Utility of major leukocyte subpopulations for monitoring secondary cytomegalovirus infections in renal-allograft recipients by PCR
AUTHOR(S): Schafer, Peter; Tenschert, Werner; Cremaschi, Liana; Gutensohn, Kai; Laufs, Rainer
CORPORATE SOURCE: Institut fur Medizinische Mikrobiologie and Immunologie, Universitats-Krankenhaus Eppendorf, Hamburg, D-20246, Germany
SOURCE: Journal of Clinical Microbiology (1998), 36(4), 1008-1014
CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The feasibility of the major peripheral blood leukocyte (PBL) subsets for use in qual. and quant. PCR to monitor secondary cytomegalovirus (**CMV**) infection and ganciclovir therapy was assessed with 188 blood samples derived from 40 **CMV** IgG-pos. renal-allograft recipients. In pp65 antigen-pos. patients all leukocyte fractions, but only 79.5% of plasma prepns., were PCR pos. In pp65 antigen-neg. samples from patients after antiviral treatment only 7.3% of polymorphonuclear cell (PMNL) samples, but 81.8% of peripheral blood mononuclear cells (PBMC), and 10.9% of plasma samples remained PCR pos. Similarly, in patients with **latent** ***infections*** only 5.0% of PMNL, but 51.7% of PBMC prepns., and 8.0% of plasma samples were PCR pos. Regarding patients with active **CMV** infection, **CMV** DNA copy nos. in PMNL correlated significantly with pp65 antigen-pos. cell counts before and after onset of ganciclovir therapy. Significant differences in **CMV** DNA copy nos. in PMNL and plasma were obsd. (i) between patients with symptomatic infection and those with asymptomatic infection and (ii) between patients with active infection and those with **latent infection**. In contrast, PBMC harbored equally low **CMV** DNA levels both in patients with active infection and those with **latent infections**, and no decline of **CMV** DNA load in PBMC was obsd. during antiviral treatment. It is concluded that detection of **CMV** DNA in PMNL, not in PBMC, is assocd. with active infections and is more sensitive than detection of **CMV** DNA in plasma. Neg. PCR results for PMNL after antiviral therapy indicate recovery, and fewer unwanted pos. results occur compared to PBMC and plasma. Therefore, purified PMNL should be preferred for anal. by qual. **CMV** PCR to avoid unwanted pos. results. The **CMV** DNA load in PBMC compared with that in PMNL is negligible during active infection, so mixed PBL are sufficient for use in quant. PCR.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:18394 CAPLUS
DOCUMENT NUMBER: 128:100526
TITLE: Cellular localization of latent murine cytomegalovirus
AUTHOR(S): Koffron, Alan J.; Hummel, Mary; Patterson, Bruce K.; Yan, Shixian; Kaufman, Dixon B.; Fryer, Jonathan P.;

Stuart, Frank P.; Abecassis, Michael I.
CORPORATE SOURCE: Department of Surgery, Division of Organ Transplantation, Northwestern University Medical School, Chicago, IL, 60611, USA
SOURCE: Journal of Virology (1998), 72(1), 95-103
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Herpesviruses typically establish **latent infection** in their hosts. The cell(s) responsible for harboring latent virus, in most cases, is not known. Using immunofluorescence and PCR-in situ hybridization (PISH), a technique which combines the sensitivity of PCR with the localization and specificity of in situ hybridization, we provide the first direct evidence that endothelial cells are a major site of murine cytomegalovirus (MCMV) DNA in latently infected animals. These findings are consistent with existing knowledge of the biol. behavior of **CMV**, in particular the transmission of latent **CMV** by solid organ and bone marrow transplantation, in both human and animal models. In addn., we have localized MCMV DNA in the lung alveolar macrophage and in bone marrow cells. Our findings confirm that bone marrow-derived hematopoietic cells are a site of ***CMV*** latency and further suggest that bone marrow may be a reservoir of infected progeny capable of migrating into the circulation and establishing latency in various tissues. These findings provide clearly needed insight into the site of **latent infection** which is central to an understanding of the mechanisms of reactivation.

L8 ANSWER 15 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:737739 CAPLUS
DOCUMENT NUMBER: 128:21302
TITLE: Differential expression of the immediate-early and early antigens in neuronal and glial cells of developing mouse brains infected with murine cytomegalovirus
AUTHOR(S): Shinmura, Yuichiro; Aiba-Masago, Sonomi; Kosugi, Isao; Li, Ren Yong; Baba, Satoshi; Tsutsui, Yoshihiro
CORPORATE SOURCE: Second Department of Pathology, Hamamatsu University School of Medicine, Hamamatsu, 431-31, Japan
SOURCE: American Journal of Pathology (1997), 151(5), 1331-1340
CODEN: AJPAA4; ISSN: 0002-9440
PUBLISHER: American Society for Investigative Pathology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Brain disorders induced by congenital cytomegalovirus (**CMV**) infection may appear at a later time after birth as a consequence of persistent infection and/or the activation of a **latent infection** of the neural cells. The authors have analyzed the infection dynamics of the neural cells in the neonatal mouse brains infected with murine **CMV** (MCMV) in the late stage of gestation. First the authors prepd. a rat monoclonal antibody to the major immediate-early (IE)-89K antigen and then used the antibody for comparison of the expression of early and late viral genes in the developing mouse brains. The cells expressing the IE-89K antigen were mostly localized in the ventricular and subventricular zones and were preferentially double stained with anti-glial fibrillary acidic protein and anti-nestin antibodies. In contrast, the cells expressing the early nuclear antigen, detected by the monoclonal antibody D5, were diffusely distributed in the cortex and the hippocampus and were mostly double labeled with anti-neuron-specific enolase antibody. In neonatal mouse brains infected congenitally with recombinant MCMV, which expressed lacZ as a late gene, the no. of the early nuclear antigen-pos. cells was much higher than that of the .beta.-galactosidase-

expressing cells, the no. of which was almost the same as that of the IE-89K antigen-pos. cells. In addn., the distribution of viral DNA-rich cells detected by DNA-DNA hybridization was similar to that of the IE-89K antigen-pos. cells. Thus, **CMV** may persistently infect neuronal cells, whereas lytic infection may preferentially occur in the glial cells in the developing brain.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:80512 CAPLUS
DOCUMENT NUMBER: 126:86809
TITLE: Latent transcripts and promoters of cytomegalovirus
INVENTOR(S): Kondo, Kazuhiro; Mocarski, Edward S., Jr.
PATENT ASSIGNEE(S): Board of Trustees of the Leland Stanford Junior University, USA; Kondo, Kazuhiro; Mocarski, Edward S., Jr.
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9637211	A1	19961128	WO 1996-US7433	19960522
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5783383	A	19980721	US 1995-450945	19950523
CA 2220415	AA	19961128	CA 1996-2220415	19960522
AU 9658017	A1	19961211	AU 1996-58017	19960522
AU 705890	B2	19990603		
EP 835122	A1	19980415	EP 1996-914744	19960522
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11507209	T2	19990629	JP 1996-535836	19960522
US 6194542	B1	20010227	US 1997-976161	19971121

PRIORITY APPLN. INFO.: US 1995-450945 A2 19950523
WO 1996-US7433 W 19960522

ABSTRACT:
The present invention provides methods and compns. relating to cytomegalovirus (**CMV**) latent transcripts, latency-assocd. polypeptides and antibodies directed against such polypeptide. The polypeptides are encoded by **CMV** DNA sequences and are produced specifically during **latent** ***infection*** . Also provided are methods of detecting **CMV** in a sample, particularly **CMV** in a latent state. The methods include RT-PCR-based methods and immunodiagnostic methods.

L8 ANSWER 17 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:668194 CAPLUS
DOCUMENT NUMBER: 125:294216
TITLE: Study on sensitivity of Southern blotting hybridization using a 32-P-labeled probe of PCR products in detecting human cytomegalovirus
AUTHOR(S): Bu, Hengfu; Chen, Juan; Shen, Rongsen; Ma, Liren; Xu, Yongqing
CORPORATE SOURCE: Laboratory Animal Centre, Academy Military Medical Sciences, Beijing, 100850, Peop. Rep. China
SOURCE: Junshi Yixue Kexueyuan Yuankan (1996), 20(2), 136-137, 140
CODEN: JYKYEL; ISSN: 1000-5501

PUBLISHER: Junshi Yixue Kexueyuan Yuankan Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
ABSTRACT:
On the basis of PCR and nested PCR for detecting human cytomegalovirus (hCMV), a 32P-labeled probe was prepd. with the amplified product of 631 bp PCR outer primers and hybridized with 300 bp inner primers amplified product. The sensitivity was increased from the previous detection limit 17 ng in 1.2% agarose electrophoresis to 500 pg by autoradiog., i.e. increased by 102 dilns. The method is able to detect less than 1 gene copy of **CMV**, thus a rapid and reliable method to detect **latent infection**.

L8 ANSWER 18 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:543553 CAPLUS
DOCUMENT NUMBER: 125:219337
TITLE: Murine cytomegalovirus DNA in peripheral blood of latently infected mice is detectable only in monocytes and polymorphonuclear leukocytes
AUTHOR(S): Mitchell, Bradley M.; Leung, Albert; Stevens, Jack G.
CORPORATE SOURCE: Dep. Microbiology and Immunology, Univ. California, Los Angeles, CA, 90024-1747, USA
SOURCE: Virology (1996), 223(1), 198-207
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Cytomegalovirus (**CMV**), as do other herpesviruses, establishes a lifelong **latent infection** in its natural host. While in immunol. intact hosts most **CMV** infections are subclin., clin. disease follows severe immunosuppression and immunodeficiency. In these situations ***CMV*** may produce serious life-threatening disease, and virus reactivated from the latent state is often responsible. Essential to understanding this virus and its pathogenesis is the need to define particular tissue and cell types harboring viral DNA. We searched for viral DNA and RNA in subpopulations of blood cells from mice latently infected with murine **CMV** by using differential centrifugation and fluorescent antibody cell sorting followed by polymerase chain reaction anal. Following i.v. inoculation, the viral DNA was found to be present in the buffy coat at and after 21 days postinfection, and both granulocytes and peripheral blood mononuclear leukocytes (PBML) were reservoirs. Further anal. of the PBML fraction by sepn. into Mac-1+ and Mac-1- cells revealed that monocytes harbored the DNA while lymphocytes were not sites of persistence. We conclude that in buffy coat of latently infected mice the viral DNA is present only in cells of the myeloid lineage. The relationship of this DNA to the **latent infection** is discussed.

L8 ANSWER 19 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:171349 CAPLUS
DOCUMENT NUMBER: 124:229598
TITLE: Anti-human cytomegalovirus activity of cytokines produced by CD4+ T-cell clones specifically activated by IE1 peptides in vitro
AUTHOR(S): Davignon, Jean-Luc; Castanie, Patrick; Yorke, Justine Allan; Gautier, Nicolas; Clement, Daniele; Davrinche, Christian
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale U 395, Centre Hospitalier Universitaire Purpan, Toulouse, 31024, Fr.
SOURCE: Journal of Virology (1996), 70(4), 2162-169
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal

LANGUAGE: English
ABSTRACT:
The control of latent cytomegalovirus (**CMV**) infections by the immune system is poorly understood. We have previously shown that CD4+ T cells specific for the human **CMV** major regulatory protein IE1 are frequent in latently infected healthy blood donors. In order to learn about the possible role of these cells, we have developed IE1-specific CD4+ T-cell clones and, in this study, analyzed their epitope specificity and function in vitro. We measured their cytokine prodn. when stimulated with specific IE1 peptides or whole recombinant IE1 protein. Their cytokine profiles, as deduced from gamma interferon (IFN-.gamma.), tumor necrosis factor alpha (TNF-.alpha.), and interleukin-4 (IL-4) and IL-6 prodn., were of the Th0- and Th1-like phenotypes. Supernatants from IE1-specific clones producing IFN-.gamma. and TNF-.alpha. were shown to inhibit **CMV** replication in U373 MG cells. This effect was due, as found by using cytokine-specific neutralizing antibodies, mostly to IFN-.gamma., which was secreted at higher levels than TNF-.alpha.. To better assess the anti-**CMV** activity of cytokines, recombinant IFN-.gamma. and TNF-.alpha. were used and shown to have a synergistic effect on the inhibition of **CMV** replication and protein expression. Thus, IE1-specific CD4+ T cells display in vitro anti-**CMV** activity through cytokine secretion and may play a role in the control of in vivo **latent** ***infections*** .

L8 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:138402 CAPLUS
TITLE: Detection of airborne cytomegalovirus in hospital rooms of immuncompromised patients
AUTHOR(S): McCluskey, Richard; Sandin, Ramon; Greene, John
CORPORATE SOURCE: Department of Pathology, Moffitt Cancer Center, University of South Florida, Tampa, FL, USA
SOURCE: Journal of Virological Methods (1996), 56(1), 115-18
CODEN: JVMEDH; ISSN: 0166-0934
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Human cytomegalovirus (**CMV**) is a major pathogen in immunocompromised patients. Transmission in this population is known to occur by fomites, but the potential for airborne spread is unkown. In this study, air from the rooms of two immunosuppressed patients with **CMV** pneumonia and one patient with **latent infection** was filtered and examd. by a polymerase chain reaction assay. **CMV**-DNA was easily detected in the rooms of the patients with pneumonia and a weak pos. signal was detected in the room of the patient with latent **CMV** infection. This technique permits the detection of aerosolized **CMV**-DNA and could possibly be adapted to detect other airborne pathogens.

L8 ANSWER 21 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:972018 CAPLUS
DOCUMENT NUMBER: 124:83586
TITLE: Molecular detection of latent murine cytomegalovirus (MCMV) DNA in hepatic sinusoidal endothelial cells
AUTHOR(S): Collins, T.; Quirk, M.; Hu, W.; Cleary, K.; Sharp, H.; Jordan, M. C.
CORPORATE SOURCE: Departments Medicine and Pediatrics, University Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Cells of the Hepatic Sinusoid (1995), 5, 37-8
CODEN: CHSIEL
PUBLISHER: Kupffer Cell Foundation
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:

Transmission of latent human cytomegalovirus (**CMV**) from donor to recipient by liver transplantation occurs at a frequency greater than with any other organ. In the murine model of **CMV**, the non-replicating ***latent*** **infection** has been characterized most extensively in the spleen where it is maintained in stromal cells within the red pulp. Using a nested polymerase chain reaction (PCR) to amplify a 200 bp region of DNA in exon 4 of the immediate early gene (IE-1), the authors have previously detected MCMV DNA in the liver of all latently infected mice. Expts. were undertaken to examine the hypothesis that latent MCMV would reside primarily in the stromal regions of the liver as in the spleen. Purified liver cell populations including hepatocytes plus sep. lymphocytes, endothelial cells, Kupffer cells, and bile duct cells were obtained by elutriation techniques from Bulb/c mice with latent MCMV infection, with DNA and RNA extd. Latent MCMV DNA was detected using the nested PCR in 10/12 samples of sinusoidal endothelial cell, 0/12 Kupffer cell, 2/6 hepatocyte, and 2/6 bile duct cell fractions (endothelial vs. Kupffer cells significant). To det. whether the lower frequency of detection of viral DNA in purified hepatocytes and bile duct cells was due to contamination with endothelial cells, combined PCR and in situ DNA hybridization was performed. Individual cell suspensions were fixed in paraformaldehyde and subjected to enzymic amplification of latent MCMV DNA. Afterwards, cell suspensions were cytocentrifuged, and the 200 bp PCR product was sought by in situ hybridization with a 35S labeled, single-stranded riboprobe. In three consecutive expts. the 200 bp PCR product was detected exclusively in sinusoidal endothelial cells. To det. whether the IE-1 gene of MCMV was expressed during latency, total RNA recovered from each liver cell population was incubated with Moloney leukemia virus reverse transcriptase and an antisense IE-1 primer to generate MCMV IE-1 cDNA. The cDNA subsequently was amplified using a nested PCR. No immediate early transcripts were detected in any liver cell population. These results indicate that latent MCMV resides within the hepatic sinusoidal endothelial cells and that the IE-1 gene is either not expressed during latency or is expressed at a level below the sensitivity of the assay used.

L8 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:698065 CAPLUS

TITLE: Analysis of target organs for the latency of murine cytomegalovirus DNA using specific pathogen free and germ-free mice

AUTHOR(S): Matsuzawa, H.; Shimizu, K.; Okada, K.; Ando, K.; Hashimoto, K.; Koga, Y.

CORPORATE SOURCE: Dep. Infectious Diseases, Univ. Sch. Med., Kanagawa, Japan

SOURCE: Archives of Virology (1995), 140(5), 853-64
CODEN: ARVIDF; ISSN: 0304-8608

PUBLISHER: Springer

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT:

Cytomegalovirus (**CMV**) establishes a **latent** ***infection*** in its host; however, the oran sites of virla latency and its mechanism still remain to be fully clarified. To elucidate this issue, a ***latent*** **infection** with murine (M) CMC was attempted to induce in mice and the organ sites of the latent viral genome were examd. for more than one yr by a plymerase chain reaction (PCR). As a result, latent MCMV DNA was detectable in both the lung and the spleen as late as 59 wks after infection. The heart was also obsd. to be a target organ of latent MCMV DNA, though the amt. of viral DNA was much less than that seen in the lung and spleen. In germ-free (GF) mice, on the other hand, no such latent viral DNA was obsd. in the spleens, while it was seen, but to a significantly smaller degree, in the lungs and the hearts than in the same organs of specific pathogen-free (SPF) mice. The amt. of infectious virions generated in the host appeared to be almost equal between the GF and SPF mice. The above findings therefore suggest that the spleen, lung and heart are target organs for MCMV

latency and the indigenous bacterial flors, which are not colonizing in GF mice, play an important role in the establishment of such viral latency in SPF mice.

L8 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:258946 CAPLUS
TITLE: Human cytomegalovirus latent infection of granulocyte-macrophage progenitors
AUTHOR(S): Kondo, Kazuhiro; Kaneshima, Hideto; Mocarski, Edward S.
CORPORATE SOURCE: Dep. Microbiol. Immunol., Stanford Univ. Sch. Med., Stanford, CA, 94305-5402, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1994), 91(25), 11879-83
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
We have investigated the interaction of human cytomegalovirus (**CMV**) with cultured primary granulocyte-macrophage progenitors, a suspected natural site of viral latency, and have established conditions for **latent** ***infection*** and reactivation in this cell population. Progenitor cells from human fetal liver or bone marrow maintained a CD14+, CD15+, CD33+ cell surface phenotye during propagation in suspension culture. Exposure to human ***CMV*** did not reduce growth or alter the phenotype of these cells during a 4-wk culture period. Viral replication was not detectable in these cells, although viral DNA, as measured by PCR anal., persisted in a high proportion of cultured cells in the absence of delayed early (.beta.) gene expression. Viral gene expression was restricted such that only ie1 region transcripts were estd. to be present in no less than 2-5% of latently infected cells. Most of these transcripts remained unspliced, a result that strikingly contrasts with the splicing pattern normally seen during viral replication in permissive cells. Latent virus reactivated after prolonged, 16- to 21-day cocultivation of infected granulocyte-macrophage progenitors with permissive cells, results that support a role for the myelomonocytic cell population as a biol. reservior of latent human **CMV** and suggest that these cells may be the source of ***CMV*** DNA PCR-pos. monocytes found in the peripheral blood of healthy carriers.

L8 ANSWER 24 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:75387 CAPLUS
DOCUMENT NUMBER: 120:75387
TITLE: The conditions of primary infection define the load of latent viral genome in organs and the risk of recurrent cytomegalovirus disease
AUTHOR(S): Reddehase, Matthias J.; Balthesen, Monika; Rapp, Maria; Jonjic, Stipan; Pavic, Ivica; Koszinowski, Ulrich H.
CORPORATE SOURCE: Inst. Microbiol., Univ. Ulm, Ulm, 89069, Germany
SOURCE: Journal of Experimental Medicine (1994), 179(1), 185-93
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Recurrence of cytomegalovirus (**CMV**) from latency is a frequent cause of disease in immunocompromised patients. To date, there is no explantation for the diversity in the clin. manifestations. Primary infection can occur perinatally or later in life, and inevitably results in **latent** ***infection*** . Seropositivity for antibodies against **CMV** is indicative of **latent infection**, but is insufficient as a predictor for the risk of recurrence. As a model for this important medical

problem, the authors compared the risks of murine **CMV** recurrence from latency established after neonatal primary infection and after infection at adult age. The risk of **CMV** recurrence was high only after neonatal infection. The copy no. of latent viral genome in tissues was identified as the key parameter that dets. the overall and organ-specific risks of recurrence. Latent **CMV** burden and risk of recurrence were related to the extent of virus multiplication during primary infection. The presence of latent **CMV** in multiple organs provides the mol. basis for stochastic events of recurrence in single organs or in any combination thereof. These findings are discussed as a concept of multifocal **CMV** latency and recurrence. It provides a rationale for the diversity in the clin. outcome of ***CMV*** disease.

L8 ANSWER 25 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:514473 CAPLUS
DOCUMENT NUMBER: 119:114473
TITLE: Dysregulation of cellular genes by latent viral genes
AUTHOR(S): Geist, Lois J.; Hunninghake, Gary W.
CORPORATE SOURCE: Univ. Iowa Hosp. Clin., Iowa City, IA, USA
SOURCE: Lung Biology in Health and Disease (1993), 65(Signal Transduction in Lung Cells), 323-34
CODEN: LBHDD7; ISSN: 0362-3181
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review, with 55 refs., on the trans-activation of cellular genes by viral gene products. The authors focus on 3 sep. virus families: the herpes viruses (HSV, **CMV**, and EBV), the retroviruses (HTLV-1 and HIV), and adenovirus. These viruses have several things in common: (1) they all cause clin. disease in the actively replicating state; (2) they all establish ***latent*** **infections**; and (3) they all express trans-acting factors now shown to interact with cellular genes.

L8 ANSWER 26 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:36890 CAPLUS
DOCUMENT NUMBER: 118:36890
TITLE: Identification and differentiation of the human herpes virus group using the PCR method
AUTHOR(S): Kawaguchi, Ryuji; Shibuya, Yoshinori; Ogasa, Utako; Kosuda, Osamu; Hikiji, Kazumasa; Ishii, Keizo
CORPORATE SOURCE: Gene Res. Lab., SRL, Inc., Hachioji, 192, Japan
SOURCE: Rinsho Byori (1992), 40(11), 1198-203
CODEN: RBYOAI; ISSN: 0047-1860
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
ABSTRACT:
Six kinds of human herpes viruses have been identified and classified on the basis of structure and characteristics using polymerase chain reaction (PCR) to amplify the virus-specific DNA sequences. This method showed higher sensitivity than the conventional method of virus isolation and culture for herpes simplex virus (HSV) and cytomegalo virus (**CMV**) detection. For each pos. control, the viral DNA was amplified only when the complementary primers themselves were used. PCR apparently detects only the activated virus, because normal controls were neg. when this method was used. Therefore, the present method is thought to closely reflect viral activation and infectious diseases in patients with **latent infections**.

L8 ANSWER 27 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:212748 CAPLUS
DOCUMENT NUMBER: 116:212748
TITLE: Gamma interferon-dependent clearance of

cytomegalovirus infection in salivary glands
AUTHOR(S): Lucin, Pero; Pavic, Ivica; Polic, Bojan; Jonjic, Stipan; Koszinowski, Ulrich H.
CORPORATE SOURCE: Fac. Med., Univ. Rijeka, Rijeka, 51000, Yugoslavia
SOURCE: Journal of Virology (1992), 66(4), 1977-84
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Cytomegalovirus (**CMV**), similar to other members of the Herpesviridae family, can establish both persistent and **latent infections**. Each of the **CMVs** that are found in many animal species replicates in the salivary gland, and oral secretion represents a source of horizontal transmission. Locally restricted replication characterizes the immunocompetent individual, whereas in the immunocompromised host, protean disease manifestations occur due to virus dissemination. The virus is cleared by immune surveillance, and CD8+ T lymphocytes play a major role. Remarkably, certain cell types of salivary gland tissues are exempt from CD8+ T-lymphocyte control of murine **CMV** infection and require the activity of CD4+ T lymphocytes. The results presented here suggest that this activity is a function of type 1 helper T-cells (Th1). Neutralization of endogenous .gamma.-interferon abrogated the antiviral activity of Th1 cells but not that of CD8+ T lymphocytes in other tissues. Neutralization of endogenous .gamma.-interferon did not interfere with the induction of the cellular and humoral immune response but acted during the effector phase. Recombinant .gamma.-interferon could not replace the function of Th1 cells in vivo and had limited direct antiviral activity in vitro. Apparently, .gamma.-interferon represents one, but not the only, essential factor involved in salivary gland clearance, establishment of **CMV** latency, and, eventually, the control of horizontal transmission.

L8 ANSWER 28 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:144860 CAPLUS
DOCUMENT NUMBER: 116:144860
TITLE: Detection of viral sequences in formalin fixed, paraffin embedded tissues from HIV-1 infected patients using the PCR
AUTHOR(S): Shibata, Darryl
CORPORATE SOURCE: Sch. Med., Univ. South. California, Los Angeles, CA, USA
SOURCE: Medical Virology (1991), 10, 55-66
CODEN: MEVIEN; ISSN: 1043-1837
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review with 51 refs. on the detection of viral nucleic acids in formalin-fixed, paraffin embedded tissues from HIV-1 infected patients using PCR. The viral DNA extd. from formalin-fixed paraffin-embedded tissues is often intact enough for restriction enzyme anal. although in many cases it is too size degraded for Southern blots. PCR can utilize this size degraded DNA as an amplification substrate and a single thin (5-10 .mu.M) section of tissue is sufficient for PCR anal. The conditions for amplification are described. Viral nucleic acids assocd. with both active and **latent** ***infections*** of HIV-1, human cytomegalovirus (**CMV**), and Epstein-Barr virus (EBV) have been detected by PCR amplification. Comparison of EBV, **CMV**, and HIV-1 infections revealed that although the nos. of HIV-1 infected cells are small, other latent viral infections are characterized by even lower levels of infection. HIV-1 apparently never establishes a true latency analogous to EBV or **CMV** since significant nos. of HIV-1 infected cells are not eliminated by the host immune response.

L8 ANSWER 29 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1991:136882 CAPLUS
DOCUMENT NUMBER: 114:136882
TITLE: A cis-acting element in the major immediate-early (IE) promoter of human cytomegalovirus is required for negative regulation by IE2
AUTHOR(S): Liu, Bo; Hermiston, Terry W.; Stinski, Mark F.
CORPORATE SOURCE: Sch. Med., Univ. Iowa, Iowa City, IA, 52242, USA
SOURCE: Journal of Virology (1991), 65(2), 897-903
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The major immediate-early promoter (MIEP) of human cytomegalovirus (**CMV**) contains a no. of different enhancer elements in both repetitive and nonrepetitive sequences that influence the level of downstream transcription. This report describes a cis-acting element in the MIEP that responds to neg. regulation by the IE2 gene product. Deletion anal. demonstrated that the cis-acting repressor element is located between the TATA box and the transcription initiation site from -13 to -1. The DNA sequence of the repressor element is 5'-CGTTTAGTGAACC-3'. The sequence is found in both the human and simian **CMV** MIEPs but not the murine **CMV** MIEP or in several other enhancer-contg. promoters. The repressor element was isolated in a DNA fragment from -13 to +3 and was found to be functional in either orientation. It could be transferred to a heterologous enhancer-contg. promoter and was functional when placed between the TATA box and the transcription initiation site. The element did not function when placed downstream of the transcription initiation site. Therefore, the cis-acting repressor element is position dependent. The role of the repressor element and the IE2 gene product in human **CMV** productive or **latent** ***infection*** is discussed.

L8 ANSWER 30 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:566231 CAPLUS
DOCUMENT NUMBER: 113:166231
TITLE: Stimulation of the human immunodeficiency virus type 2 (HIV-2) gene expression by the cytomegalovirus and HIV-2 transactivator gene
AUTHOR(S): Arya, Suresh K.; Sethi, Anita
CORPORATE SOURCE: Lab. Tumor Cell Biol., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SOURCE: AIDS Research and Human Retroviruses (1990), 62(5), 649-58
CODEN: ARHRE7; ISSN: 0889-2229
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Human immunodeficiency virus (HIV) often causes **latent** ***infection*** . Transactivation by some DNA virus has been implicated in inducing HIV-1 replication and pathogenesis. The transactivator (IE-2) gene of the human cytomegalovirus (**CMV**) can enhance HIV-2 as well as HIV-1 gene expression in vitro. This inducer can act in concert with the HIV-2 tat gene and T-cell activation in enhancing gene expression in human CD4+ lymphocytes. While the HIV-2 and HIV-1 tat genes and T-cell activators apparently employ independent modes of action, the **CMV** transactivator in combination with the HIV-2 tat or T-cell activators may employ a gene activation pathway with some common and some distinct components. Both HIV-2 and **CMV** transactivators enhance HIV-2 gene expression by transcriptional activation involving transcript initiation as well as elongation, with **CMV** transactivator affecting elongation more than the initiation. A significant proportion of transcripts appear to terminate prematurely in the absence of transactivators. Deletion mutation anal. of the HIV-2 long terminal repeat (LTR) suggests that the element that responds to ***CMV*** transactivation in human CD4+ lymphocytes is either a diffuse one

or located downstream of the HIV-2 enhancer element.

L8 ANSWER 31 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1977:546454 CAPLUS
DOCUMENT NUMBER: 87:146454
TITLE: Reactivation of murine cytomegalovirus by cyclophosphamide
AUTHOR(S): Mayo, Donald R.; Armstrong, John A.; Ho, Monto
CORPORATE SOURCE: Grad. Sch. Public Health, Univ. Pittsburgh, Pittsburgh, PA, USA
SOURCE: Nature (London, United Kingdom) (1977), 267(5613), 721-3
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Latent mouse cytomegalovirus (MCMV) infection in DBA/2 mice was reactivated by cyclophosphamide (I) [50-18-0] (150 mg/kg, 2 or 3 doses, 5-6 days apart). MCMV was found almost exclusively in salivary gland. This **latent** ***infection*** was also reactivated in other animals after transfer of latently-infected spleen cells. With allogeneic recipients, infection due to reactivation of donor cells was more frequent in I-treated mice than in untreated animals. The mouse/MCMV system may be an excellent model for human ***CMV*** infections in transplant recipients.

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:796011 CAPLUS
DOCUMENT NUMBER: 138:218045
TITLE: The genes encoding the gCIII complex of human cytomegalovirus exist in highly diverse combinations in clinical isolates
AUTHOR(S): Rasmussen, Lucy; Geissler, Aimee; Cowan, Catherine; Chase, Amanda; Winters, Mark
CORPORATE SOURCE: Dep. Med., Stanford Univ. Sch. Med., Stanford, CA, 94305, USA
SOURCE: Journal of Virology (2002), 76(21), 10841-10848
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The UL74 (**glycoprotein O** [gO])-UL75 (gH)-UL115 (gL) complex of human cytomegalovirus (**CMV**), known as the gCIII complex, is likely to play an important role in the life cycle of the virus. The gH and gL proteins have been assocd. with biol. activities, such as the induction of virus-neutralizing antibody, cell-virus fusion, and cell-to-cell spread of the virus. The sequences of the 2 gH gene variants, readily recognizable by restriction endonuclease polymorphism, are well conserved among clin. isolates, but nothing is known about the sequence variability of the gL and gO genes. Sequencing of the full-length gL and gO genes was performed with 22-39 clin. isolates, as well as with lab. strains AD169, Towne, and Toledo, to det. phylogenetically based variants of the genes. The sequence information provided the basis for identifying gL and gO variants by restriction endonuclease polymorphism. The predicted gL amino acid sequences varied <2% among the isolates, but the variability of gO among the isolates approached 45%. The variants of the genes coding for gCIII in lab. strains Towne, AD169, and Toledo were different from those in most clin. isolates. When clin. isolates from different patient populations with various degrees of symptomatic ***CMV*** disease were surveyed, the gO1 variant occurred almost exclusively with the gH1 variant. The gL2 variant occurred with a significantly lower frequency in the gH1 variant group. There were no configurations of the gCIII complex that were specifically assocd. with symptomatic **CMV** disease or human immunodeficiency virus serol. status. The potential for the gCIII complex to exist in diverse genetic combinations in clin. isolates points to a new aspect that must be considered in studies of the significance of ***CMV*** strain variability.

L6 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:620269 CAPLUS
DOCUMENT NUMBER: 129:326815
TITLE: The human **cytomegalovirus** UL74 gene encodes the third component of the glycoprotein H-glycoprotein L-containing envelope complex
AUTHOR(S): Huber, Mary T.; Compton, Teresa
CORPORATE SOURCE: Program in Cellular and Molecular Biology and Department of Medical Microbiology and Immunology, University of Wisconsin-Madison, Madison, WI, 53706-1532, USA
SOURCE: Journal of Virology (1998), 72(10), 8191-8197
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The human **cytomegalovirus** (HCMV) gCIII envelope complex is composed of glycoprotein H (gH; gpUL75), glycoprotein L (gL; gpUL115), and a third, 125-kDa protein not related to gH or gL (M. T. Huber and T. Compton, J. Virol. 71:5391-5398, 1997; L. Li, J. A. Nelson, and W. J. Britt, J. Virol. 71:3090-3097, 1997). Glycosidase digestion anal. demonstrated that the 125-kDa protein was a glycoprotein contg. ca. 60 kDa of N-linked oligosaccharides on a peptide backbone of 65 kDa or less. Based on these biochem. characteristics, two HCMV open reading frames, UL74 and TRL/IRL12, were identified as candidate genes for the 125-kDa glycoprotein. To identify the gene encoding the 125-kDa glycoprotein, the authors purified the gCIII complex, sepd. the components by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, and subjected gH and the 125-kDa glycoprotein to amino acid microsequence anal. Microsequencing of an internal peptide derived from purified 125-kDa glycoprotein yielded the amino acid sequence LYVGPTK. A FASTA search revealed an exact match of this sequence to amino acids 188 to 195 of the predicted product of the candidate gene UL74, which we have designated **glycoprotein O** (gO).
Anti-gO antibodies reacted in immunoblots with a protein species migrating at ca. 100 to 125 kDa in lysates of HCMV-infected cells and with 100- and 125-kDa protein species in purified virions. Anti-gO antibodies also immunopptd. the gCIII complex and recognized the 125-kDa glycoprotein component of the gCIII complex. Positional homologs of the UL74 gene were found in other betaherpesviruses, and comparisons of the predicted products of the UL74 homologs genes demonstrated a no. of conserved biochem. features

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:173513 CAPLUS
DOCUMENT NUMBER: 136:366301
TITLE: A role for human **cytomegalovirus** **glycoprotein O** (gO) in cell fusion and a new hypervariable locus
AUTHOR(S): Paterson, David A.; Dyer, Angela P.; Milne, Richard S. B.; Sevilla-Reyes, Edgar; Gompels, Ursula A.
CORPORATE SOURCE: Pathogen Molecular Biology and Biochemistry Unit, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, University of London, London, WC1E 7HT, UK
SOURCE: Virology (2002), 293(2), 281-294
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A cell fusion assay using fusion-from-without (FFWO) recombinant adenoviruses (RAds) and specific antibody showed a role in fusion modulation for glycoprotein gO, the recently identified third component of the gH/gL gCIII complex of human **cytomegalovirus** (HCMV). As in HCMV, RAd gO expressed multiple glycosylated species with a mature product of 125 kDa. Coexpression with gH/gL RAds showed gCIII reconstitution in the absence of other HCMV products and stabilization by intermol. disulfide bonds. Properties of HCMV clin. isolate, Pt, also implicated gO in cell spread. Compared to lab. strain AD169, Pt was resistant to gH antibody plaque inhibition, but mature gH was identical. However, the gO sequences were highly divergent (20%), with further variation in lab. strain Towne gO (34%). Thus, gO forms gCIII with gH/gL, performs in cell fusion, and is a newly identified HCMV hypervariable locus which may influence gCIII's function in mediating infection.